STRUCTURE SEARCH


```
=> file reg
FILE 'REGISTRY' ENTERED AT 15:50:40 ON 05 JUL 2005
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STRUCTURE FILE UPDATES:     4 JUL 2005  HIGHEST RN 853727-85-2
DICTIONARY FILE UPDATES:    4 JUL 2005  HIGHEST RN 853727-85-2

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 15:50:49 ON 05 JUL 2005
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FILE COVERS 1907 - 5 Jul 2005  VOL 143 ISS 2
FILE LAST UPDATED: 4 Jul 2005  (20050704/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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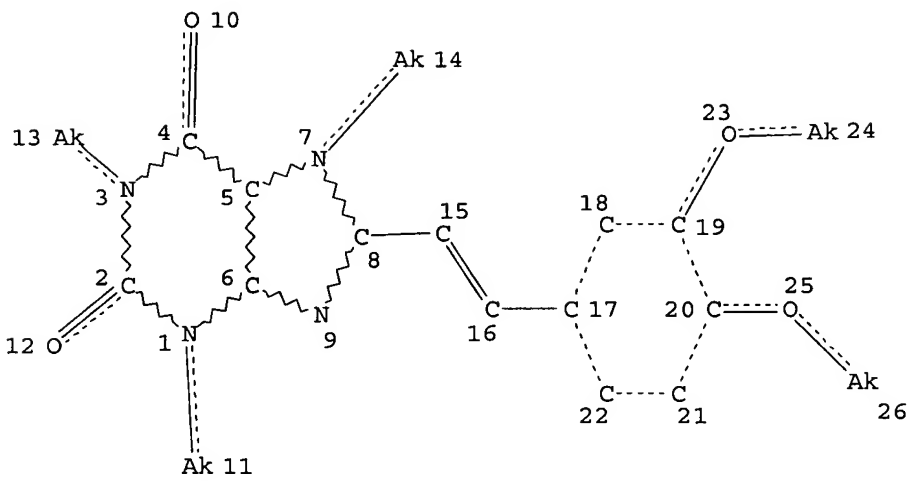
=> d que L19
L7 STR



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DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 10 11 12 13 14 15 16 23 24 25 26
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L10 104 SEA FILE=REGISTRY SSS FUL L7

L15 96 SEA FILE=CAPLUS ABB=ON PLU=ON L10 (L) (BAC OR DMA OR PAC OR PKT OR THU)/RL
L16 28818 SEA FILE=CAPLUS ABB=ON PLU=ON (ISCHEMIA/CT OR "BLOOD VESSEL, DISEASE (L) ISCHEMIA"/CT OR "ISCHEMIA CARDIOVASCULAR SYSTEM"/CT OR "BRAIN (L) CEREBRAL CORTEX, ISCHEMIA"/CT OR "BRAIN (L) HIPPOCAMPUS, ISCHEMIA"/CT OR "BRAIN (L) HIPPOCAMPUS, SECTOR CA1, ISCHEMIA"/CT OR "BRAIN (L) HIPPOCAMPUS, SECTOR CA1, PYRAMIDAL CELL LAYER, ISCHEMIA"/CT OR "BRAIN (L) ISCHEMIA"/CT OR "BRAIN (L) ISCHEMIA, FOCAL"/CT OR "BRAIN (L) ISCHEMIA, TRANSIENT"/CT OR "BRAIN (L) PROSENCEPHALON, ISCHEMIA"/CT OR "BRAIN (L) PROSENCEPHALON, ISCHEMIA, TRANSIENT"/CT OR "BRAIN (L) STRIATUM, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) FOREBRAIN, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) HIPPOCAMPUS, SECTOR CA1, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) HIPPOCAMPUS, SECTOR CA1, PYRAMIDAL CELL LAYER, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) ISCHEMIA"/CT OR "BRAIN, DISEASE (L) PROSENCEPHALON, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) PROSENCEPHALON, ISCHEMIA, TRANSIENT"/CT)
L17 4338 SEA FILE=HCAPLUS ABB=ON PLU=ON ("ANTI-ISCHEMIC AGENTS"/CT OR "ANTI-ISCHEMIA AGENTS"/CT OR "ANTI-ISCHEMIC DRUGS"/CT OR "ANTIISCHEMIA AGENTS"/CT OR "ANTIISCHEMIC AGENTS"/CT OR ANTIISCHEMICS/CT)
L19 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (L16 OR L17 OR BRAIN?)

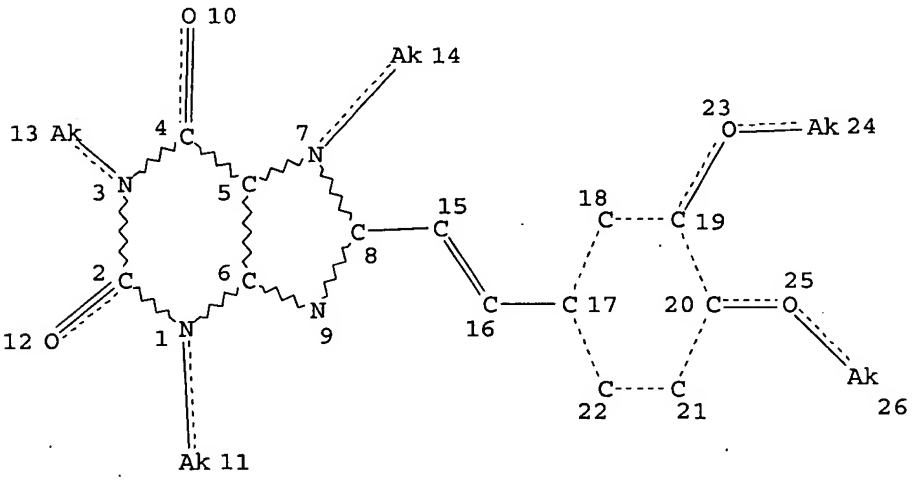
=> file embase
FILE 'EMBASE' ENTERED AT 15:51:09 ON 05 JUL 2005

FILE COVERS 1974 TO 30 Jun 2005 (20050630/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que L29
L7 STR



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DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  10 11 12 13 14 15 16 23 24 25 26
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  26

STEREO ATTRIBUTES: NONE
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L26          169 SEA FILE=EMBASE ABB=ON  PLU=ON  L10
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                 INSUFFICIENCY"/CT OR "BRAIN CIRCULATION DISORDER"/CT OR "BRAIN
                 ISCHAEMIA"/CT OR "BRAIN ISCHEMIA-HYPOXIA"/CT OR "CEREBRAL
                 BLOOD CIRCULATION DISORDER"/CT OR "CEREBRAL BLOOD FLOW
                 DISORDER"/CT OR "CEREBRAL CIRCULATION DISORDER"/CT OR "CEREBRAL
                  ISCHAEMIA"/CT OR "CEREBRAL ISCHEMIA"/CT OR "CEREBROVASCULAR
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                 "CEREBROVASCULAR ISCHEMIA"/CT OR "HYPOXIA-ISCHEMIA, BRAIN"/CT
                 OR "ISCHAEMIC BRAIN DISEASE"/CT OR "ISCHEMIA CEREBRI"/CT OR
                 "ISCHEMIC BRAIN DISEASE"/CT OR "ISCHEMIC ENCEPHALOPATHY"/CT OR
                 "NEURAL ISCHEMIA"/CT OR "BRAIN VASOSPASM"/CT OR "TRANSIENT
                 ISCHEMIC ATTACK"/CT)
L28        53061 SEA FILE=EMBASE ABB=ON  PLU=ON  L27 OR  BRAIN(5A)(?ISCHEM? OR
                 ?INFARC? OR ?HYPOX? OR ?NEURODEGEN?)
L29            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L26 AND L28


=> file stng
FILE 'STNGUIDE' ENTERED AT 15:51:42 ON 05 JUL 2005
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jul 1, 2005 (20050701/UP).

=> dup remove L19 L29
FILE 'HCAPLUS' ENTERED AT 15:52:02 ON 05 JUL 2005

FILE 'EMBASE' ENTERED AT 15:52:02 ON 05 JUL 2005

PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L29
L34 40 DUP REMOVE L19 L29 (0 DUPLICATES REMOVED)

=> d ibib abs hitind hitstr 1-40 L34

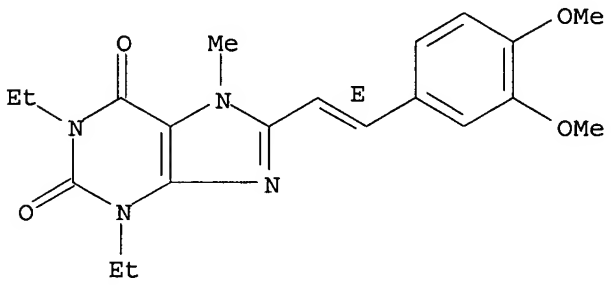
L34 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:646209 HCAPLUS
DOCUMENT NUMBER: 142:211382
TITLE: Novel Diamino Derivatives of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as Potent and Selective Adenosine A2a Receptor Antagonists
AUTHOR(S): Vu, Chi B.; Pan, Deborah; Peng, Bo; Kumaravel, Gnanasambandam; Smits, Glenn; Jin, Xiaowei; Phadke, Deepali; Engber, Thomas; Huang, Carol; Reilly, Jennifer; Tam, Stacy; Grant, Donna; Hetu, Gregg; Petter, Russell C.
CORPORATE SOURCE: Department of Medicinal Chemistry, Biogen Idec Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 2009-2018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Piperazine derivs. of 2-furanyl[1,2,4]triazolo[1,5-a][1,3,5]triazine have recently been demonstrated to be potent and selective adenosine A2a receptor antagonists with oral activity in rodent models of Parkinson's disease. We have replaced the piperazinyl group with a variety of linear, monocyclic, and bicyclic diamines. Of these diamines, (R)-2-(aminomethyl)pyrrolidine is a particularly potent and selective replacement for the piperazinyl group. With this diamine component, we have been able to prepare numerous analogs with low nanomolar affinity toward the A2a receptor and good selectivity with respect to the A1 receptor (>200-fold in some cases). Selected analogs from this series of [1,2,4]triazolo[1,5-a][1,3,5]triazine have now been shown to be orally active in the mouse catalepsy model.
CC 1-3 (Pharmacology)
Section cross-reference(s): 2, 14
IT **Brain**
(cerebral cortex; novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)
IT 139180-30-6, ZM-241385 **155270-99-8**, KW-6002 160098-96-4, SCH-58261 745072-66-6

RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)

IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)

RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:214290 HCAPLUS
DOCUMENT NUMBER: 142:404037
TITLE: KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse
AUTHOR(S): Pierri, Mette; Vaudano, Elisabetta; Sager, Thomas; Englund, Ulrica
CORPORATE SOURCE: H. Lundbeck A/S, Pharmacology Target Research, Valby, DK-2500, Den.
SOURCE: Neuropharmacology (2005), 48(4), 517-524
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The risk of Parkinson's disease (PD) is associated with a lower intake of caffeine, a non-selective adenosine A2A antagonist. In agreement, genetic or pharmacol. inactivation of adenosine A2A receptors in animal models of PD has demonstrated both symptomatic and neuroprotective effects. These findings and the lack of disease modifying therapies have led to intense research on adenosine A2A antagonists as a novel treatment for PD. In the present study the neuroprotective effect of the A2A receptor antagonist KW-6002 was investigated using different models of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in mice, which induced dopaminergic terminal and or dopaminergic cell loss and inflammation. Treatment with KW-6002 prevented the loss of dopaminergic striatal terminals and nigral cell bodies and inhibited the nigral microglia activation. Our results confirm previous findings that pharmacol. inactivation of A2A receptors inhibits MPTP-induced dopaminergic damage at the level of striatum. In addition, we demonstrate for the first time that, after MPTP treatment in

mice, an A2A antagonist is neuroprotective, and has anti-inflammatory effects, at the level of the substantia nigra. Thus, our data further support the use of A2A receptor antagonists as a novel neuroprotective therapy for PD.

CC 1-11 (Pharmacology)

IT Anti-inflammatory agents
Brain
(substantia nigra; KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

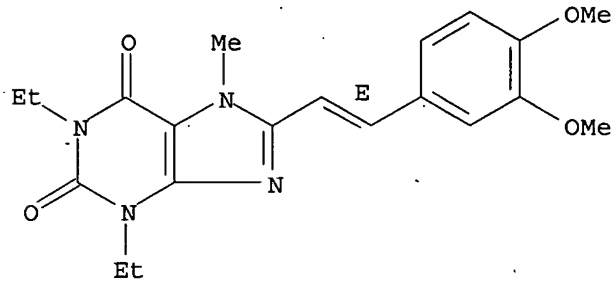
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:570030 HCAPLUS
DOCUMENT NUMBER: 141:99661
TITLE: Identification of compounds suitable as agonists and/or antagonists of adenosine A2A receptor coupled to specific G proteins, and use of identified compounds in treatment of various disorders in mammals
INVENTOR(S): Fredholm, Bertil B.; Kull, Bjoern
PATENT ASSIGNEE(S): Actar Ab, Swed.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058974	A1	20040715	WO 2003-SE2086	20031229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,				

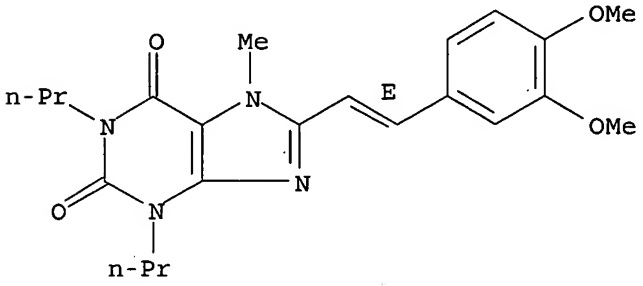
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-436480P P 20021227

AB The invention discloses a method of drug screening to select chemical compds. suitable as receptor agonists or antagonists that act on a receptor belonging to the family of G protein coupled receptors. The method involves constructing a biol. preparation comprising a receptor coupled to a specific G protein, bringing a compound in contact with said preparation, and studying the functional properties of said compound in biol. preparation The invention also discloses the use of identified compound as a drug for treatment of CNS disorders, cardiovascular disorders, inflammatory disorders, metabolic disorders, cancer and other hyperproliferative disorders in a mammal. Specifically, the invention discloses a novel approach to identify and test compds. based on changes in adenosine A2A receptor binding dependent on the nature of the coupled G protein. The invention related that this approach seemed feasible due to the evidence that G proteins, such as Gs, Gi or Golf, influence the binding properties of A2A receptors. The invention also related that a truly efficient drug mol., in addition to affinity towards A2A, can be specific towards the different G proteins associated with A2A. In the examples, the invention used transformed CHO cells expressing A2A receptors linked to Gs or Golf G proteins, and demonstrated the existence of G-protein-dependent ligand specificity. Specifically, the examples demonstrated that substance KF 17837 has higher affinity to the A2A-Golf complex in striatum than to A2A-Gs complex in leukocytes. The examples also showed how some compds. influence A2A receptors coupled to Golf more readily than A2A receptors coupled to Gs.

IC ICM C12N015-12
ICS G01N033-53; C12Q001-68; C07K014-705; A61P025-16; A61P037-00
CC 1-1 (Pharmacology)
Section cross-reference(s): 2, 14
IT Lymphocyte
(binding of chemical compds. to adenosine A2A receptors in membrane preparation
derived from pig **brain** (A2A receptors coupled to Golf) or
from pig lymphocytes (A2A receptors coupled to Gs))
IT **Brain**
(corpus striatum; binding of chemical compds. to adenosine A2A receptors in membrane preparation derived from pig **brain** (A2A receptors coupled to Golf) or from pig lymphocytes (A2A receptors coupled to Gs))
IT 146-77-0 446-72-0 17318-31-9 18732-09-7 18732-18-8 20125-40-0
35788-27-3 46155-90-2 53296-10-9 91896-57-0 126235-09-4
141018-30-6 144930-92-7 380878-34-2 381701-48-0 400087-52-7
721401-37-2 721401-39-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of chemical compds. to adenosine A2A receptors in membrane preparation
derived from pig **brain** (A2A receptors coupled to Golf) or
from pig lymphocytes (A2A receptors coupled to Gs))
IT **141807-96-7**, KF 17837
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance KF 17837 has higher affinity to A2A receptor -Golf complex

in striatum than to A2A-Gs complex in leukocytes)
IT **141807-96-7**, KF 17837
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance KF 17837 has higher affinity to A2A receptor -Golf complex in striatum than to A2A-Gs complex in leukocytes)
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:566535 HCAPLUS
DOCUMENT NUMBER: 141:99728
TITLE: A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral disorders
INVENTOR(S): Shiozaki, Shizuo; Shimada, Junichi; Kase, Hiroshi; Shindo, Mayumi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

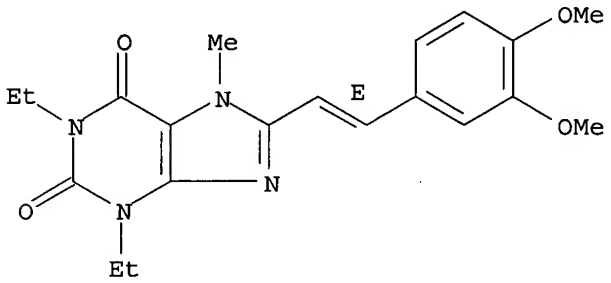
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	20031224
WO 2004058139	A3	20041104		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-509039P P 20021227
AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also

be used for Tic/Tourette's disorder.
IC ICM A61K
CC 1-11 (Pharmacology)
IT **Brain**, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine derivative for treatment of behavioral disorders)
IT **155270-99-8**
RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)
IT **155270-99-8**
RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:522325 HCAPLUS
DOCUMENT NUMBER: 141:99592
TITLE: Adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease
AUTHOR(S): Ochi, M.; Shiozaki, S.; Kase, H.
CORPORATE SOURCE: Pharmaceutical Research Institute, Ltd, Kyowa Hakko Kogyo Co., Shizuoka, 411-8731, Japan
SOURCE: Neuroscience (Oxford, United Kingdom) (2004), 127(1), 223-231
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A target neuron of adenosine A2A receptor antagonists to exert anti-parkinsonian activities has been currently identified to be, at least in part, striatopallidal medium spiny neurons (MSNs). In the present study, we determine whether A2A receptor-mediated modulation is associated with changes in the release of GABA and glutamate in the substantia nigra pars reticulata (SNr), an output structure of the whole basal ganglia network, using in vivo microdialysis in a rat Parkinson's disease (PD) model. In 6-hydroxydopamine (OHDA)-lesioned rats compared with normal rats, basal extracellular GABA levels in the SNr show no change, whereas basal glutamate levels are significantly increased. Oral administration of the A2A receptor-selective antagonist E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-

methyl-3,7-dihydro-1-H-purine-2,6-dion (KW-6002) to 6-OHDA-lesioned rats at 1 mg/kg caused a marked and sustained increase of GABA and glutamate levels in the SNr. The increase of nigral glutamate by KW-6002 was abolished by a kainic acid-induced lesion of the globus pallidus (GP) or subthalamic nucleus (STN) in 6-OHDA-lesioned rats, whereas the increase of nigral GABA was completely blocked by the GP-lesion but only partially blocked by the STN-lesion. These results indicate that changes in neurotransmitter release in the SNr brought about by KW-6002 are largely attributable to blockade of A2A receptor-mediated modulation of striatopallidal MSNs. Thus, these actions of KW-6002 on striatopallidal MSNs may be the main mechanism for ameliorating PD by A2A antagonists.

CC 1-11 (Pharmacology)

ST Parkinsonism **brain** GABA glutamate adenosine A2A KW6002

IT **Brain**
(substantia nigra, pars reticulata; adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

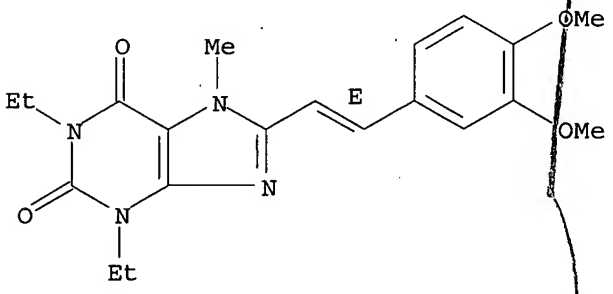
IT **155270-99-8**, KW-6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

IT **155270-99-8**, KW-6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2004441787 EMBASE

TITLE: List of drugs in development for neurodegenerative diseases: Update June 2004.

AUTHOR: Kwon M.-O.; Fischer F.; Matthisson M.; Herrling P.

CORPORATE SOURCE: Prof. P. Herrling, Novartis International AG, Postfach,

CH-4002 Basel, Switzerland. Paul.Herrling@group.novartis.co
m
SOURCE: Neurodegenerative Diseases, (2004) Vol. 1, No. 2-3, pp. 113-152.
ISSN: 1660-2854 CODEN: NDEIA6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20050414
Last Updated on STN: 20050414

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

CT Medical Descriptors:
*degenerative disease: DT, drug therapy
drug effect
schizophrenia: DT, drug therapy
pain: DT, drug therapy
Alzheimer disease: DT, drug therapy
anxiety disorder: DT, drug therapy
psychosis: DT, drug therapy
sleep disorder: DT, drug therapy
major depression: DT, drug therapy
dementia: DT, drug therapy
schizoaffective psychosis: DT, drug therapy
Huntington chorea: DT, drug therapy
brain ischemia: DT, drug therapy
incontinence: DT, drug therapy
asthma: DT, drug therapy
central nervous system disease: DT, drug therapy
mental disease: DT, drug therapy
spinal cord injury: DT, drug therapy
brain disease: DT, drug therapy
attention deficit disorder: DT, drug therapy
epilepsy: DT, drug therapy
head injury: DT, drug therapy
liver cirrhosis: DT, drug therapy
cancer: DT, drug therapy
neuropathy: DT, drug therapy
multiple sclerosis: DT, drug therapy
neurotoxicity: DT, drug therapy
drug induced disease: DT, drug therapy
inflammation: DT, drug therapy
immune deficiency: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
chronic obstructive lung disease: DT, drug therapy
enteritis: DT, drug therapy
mood disorder: DT, drug therapy
coughing: DT, drug therapy
glaucoma: DT, drug therapy
motor neuron disease: DT, drug therapy
cognitive defect: DT, drug therapy
Parkinson disease: DT, drug therapy
migraine: DT, drug therapy
restenosis: DT, drug therapy
heart infarction: DT, drug therapy
autoimmune disease: DT, drug therapy

ulcerative colitis: DT, drug therapy
respiratory distress syndrome: DT, drug therapy
systemic lupus erythematosus: DT, drug therapy
nervous system injury: DT, drug therapy
liver disease: DT, drug therapy
senile arch: DT, drug therapy
prostate tumor: DT, drug therapy
drug mechanism
drug indication
human
review
priority journal
Drug Descriptors:
neuroleptic agent: DT, drug therapy
neuroleptic agent: PD, pharmacology
analgesic agent: DT, drug therapy
analgesic agent: PD, pharmacology
nootropic agent: DT, drug therapy
nootropic agent: PD, pharmacology
neuroprotective agent: DT, drug therapy
neuroprotective agent: PD, pharmacology
anticonvulsive agent: DT, drug therapy
anticonvulsive agent: PD, pharmacology
anxiolytic agent: DT, drug therapy
anxiolytic agent: PD, pharmacology
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
antidepressant agent: DT, drug therapy
antidepressant agent: PD, pharmacology
muscle relaxant agent: DT, drug therapy
muscle relaxant agent: PD, pharmacology
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
antiinflammatory agent: DT, drug therapy
antiinflammatory agent: PD, pharmacology
antihypertensive agent: DT, drug therapy
antihypertensive agent: PD, pharmacology
immunomodulating agent: DT, drug therapy
immunomodulating agent: PD, pharmacology
spasmolytic agent: DT, drug therapy
spasmolytic agent: PD, pharmacology
antiarrhythmic agent: DT, drug therapy
antiarrhythmic agent: PD, pharmacology
antitussive agent: DT, drug therapy
antitussive agent: PD, pharmacology
serotonin 2A antagonist: DT, drug therapy
serotonin 2A antagonist: PD, pharmacology
cyclooxygenase 2 inhibitor: DT, drug therapy
cyclooxygenase 2 inhibitor: PD, pharmacology
monoamine oxidase B inhibitor: DT, drug therapy
monoamine oxidase B inhibitor: PD, pharmacology
adenosine kinase inhibitor: DT, drug therapy
adenosine kinase inhibitor: PD, pharmacology
dopamine 3 receptor blocking agent: DT, drug therapy
dopamine 3 receptor blocking agent: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
calpastatin: DT, drug therapy
calpastatin: PD, pharmacology

glycine receptor antagonist: DT, drug therapy
glycine receptor antagonist: PD, pharmacology
muscarinic M1 receptor agonist: DT, drug therapy
muscarinic M1 receptor agonist: PD, pharmacology
antiparkinson agent: DT, drug therapy
antiparkinson agent: PD, pharmacology
AMPA receptor antagonist: DT, drug therapy
AMPA receptor antagonist: PD, pharmacology
dopamine 2 receptor blocking agent: DT, drug therapy
dopamine 2 receptor blocking agent: PD, pharmacology
nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor: DT, drug therapy
nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor: PD, pharmacology
unindexed drug
remacemide
selegiline

CT Drug Descriptors:
zydis
7b12
2 methyl 3 (2 pyrrolidinylmethoxy)pyridine
abs 205
a 72055
a 366833
a 35380
a 134974
ac 184897
ac 90222
6,7 dichloro 5 nitro 2,3 quinoxalinedione
acp 103
acpc
ad gl0002
aeg 3482
aeol 10150
agy 110
agy 207
ak 275
vasolex
alaptid
n (2 hydroxyethylamino) 3 nitronaphthalimide
altropane
am 36
donepezil
ampakines
Alzheimer disease vaccine
anatibant
apbpi 124
ar 139525
ar 15896
ar a 008055
spiro[1 azabicyclo[2.2.2]octane 3,2' thiazolidine] 2' one
ar r 18565
arry 142886
arx 2000
arx 2001
arx 2002
asenapine
aptiganel
as 600292

lanicemine
as 004509
as 601245
av 201
avp 923
recombinant ciliary neurotrophic factor
az 36041
azd 0328
ba 1016
bay 38 7271
bay x 9227
bd 1054
besonprodil
bgc 20 1178
1 (3,4 dihydroxy 5 nitrophenyl) 2 phenylethanone
bifeprunox
biii 890 cl
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide
bls 602
blonanserin
alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol
brasofensine
breflate
bls 605
bts 72664
bvt 2989
bxt 51072
cdd 0304
cee 03 310
cee 03 320
cep 1347
cep 3122
cep 4186
cep 751
cere 20
cere 130
cere 120
3 aminopropyl(diethoxymethyl)phosphinic acid
chf 2060
chf 3381
ckd 705
cnic 568
cns 2103
cns 5065
colostrinin
cp 132484
cp 283097
cp 465022
cpc 304
6 quinoxalinecarboxylic acid piperidide
dabelotine
dar 201
2 (2,3 dicarboxycyclopropyl)glycine
dd 20207
3,3 bis(3 fluorophenyl) n methylpropylamine
delucemine
10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone
novasite

dp 103
dp 109
dp b99
dpp 225
dr 2313
dy 9760c
e 2007
e 2051
e 2101
eaa 494
midafotel
eab 318
ect ad
ect pd
norphenazone
ef 7412
egis 7444
CT Drug Descriptors:
eht 202
tsukubaenolide
eliprodil
eht 201
pentoxifylline
aloxistatin acid
eqa 00
Polypodium leucotomos extract
3,3',4,4' tetrahydro 6,6',8,8' tetramethoxy 3,3' dimethyl[10,10' bi 2 oxanthracene] 4,9,9' (1h,1'h) triol 4 acetate
f 10981
f 2 ccg i
fce 29484a
fce 29642a
ersofermin
ascomycin
n (4 acetyl 1 piperazinyl) 4 fluorobenzamide
flindokalner
formobactin
fpl 16283
fr 210575
galdansetron
ganstigmine
liatermine
gke 841
glialines
throphix
gmc 1111
gp 14683
gpi 1485
gr 1485
5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]
gt 2342
gt 715
gv 2400
1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine
hf 0220
hp 184
ica 69673
idn 6556
ifenprodil

igt 440103
ino 1001
ipenoxazone
isp 1
clk 1
it 657
kf 17329
pralmorelin
krp 199
krx 411
istradefylline
l 687306
3 amino 1 hydroxy 4 methyl 2 pyrrolidinone
5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid
l 701252
lamotrigine
lau 0501
lau 8080
lax 101
lentivector
leteprinim
liga 20
5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone
decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid
decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3 isoquinolinecarboxylic acid
ly 302427
ly 354006
2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid
ly 451395
ly 483518
m 40401
mcc 257
4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine
4 carboxymethylamino 5,7 dichloro 2 quinolinecarboxylic acid
3,4 dihydro 3,3 dimethylisoquinoline 2 oxide
mdl 102288
3 (2 carboxy 2 phenylethenyl) 4,6 dichloro 1h indole 2 carboxylic acid
5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one
[1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester
3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid
recombinant somatomedin C
mem 1003
pramipexole
mito 4509
mito 4565
2 (2 oxo 1 pyrrolidinyl) n (5,6,7,8 tetrahydro 2,3 dimethylfuro[2,3 b]quinolin 4 yl)acetamide
lactacystin beta lactone
icosapentaenoic acid ethyl ester
ms 153
mt 5
n 3393
nbi 30702
nc 531
2 [4 methoxy 3 (2 phenylethoxy)phenyl] n,n dipropylethylamine
neramexane

neublastin
neurocale
neurostrol
neurovex
clomethiazole
5 (2 chloro 1 hydroxyethyl) 4 methylthiazole
nnc 07 0775
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione
noggin
norleu
nox 700
3 amino 1,1 bis(3 fluorophenyl)butane
nps 846
nrt 115
ns 1209
ns 1608
ns 2330
ns 257
ns 377
ns 638
CT Drug Descriptors:
ns 649
nt 4
nt 5
nw 1048
nxd 5150
nxd 9062
4 [(tert butylimino)methyl] 1,3 benzenedisulfonate disodium n oxide
ono 2506
n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide
org 24448
p 58
p 9939
pan 811
pbt 1
pd 132026
pd 148903
pd 150606
pd 159265
pd 90780
pdc 008 004
pe21
perzinfotel
pn 277
pn 401
pnu 87663
2 dipropylamino 5,6 dimethoxyindan
6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole
pnu 157678
pnu 170413
pnu 177864
pol 255
ppi 368
pre 103
prs 211220
pti 777
pym 50018

pym 50028
qg 2283
qr 333
r 1485
r 1577
ren 1654
ren 1820
rg 1068
ri 820
rjr 1401
2 (3 pyridinyl)quinuclidine
ro 09 2210
geomatrix
rpr 104632
rs 100642
s 312 d
s 1746
7 dipropylamino 2,3,5,6,7,8 hexahydronaphtho[2,3 b]furan
s 14820
s 176251
s 34730 1
s 34730
s 18986
s 33113 1
s 33138
sarizotan
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole
5 chloro n [4 methoxy 3 (1 piperazinyl)phenyl] 3 methyl 2
benzothiophenesulfonamide
n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4
quinolinecarboxamide
sca 136
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5
c]pyrimidine
sea 0400
semax
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate
siclofen
sgs 518
sja 6017
2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine
skf 74652
3 allyl 6 chloro 2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3
benzazepine
sl 340026
sl 65 0155
7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone
slv 314
slv 319
sm 13496
SNX 482
sp (v5.2)c
spc 9766
sph 1371
spm 914
spm 935
sr 57667
sra 333

ssr 125047
ssr 146977
ssr 180575
ssr 181507
ssr 482073
ssr 504734
sumanirole
5 [3 [4 (4 fluorophenyl) 1 piperazinyl]propyl] 1,4,5,6,7,8 hexahydro 8 hydroxy 1 methylpyrrolo[3,2 c]azepin 4 one
sun n8075
survivins
sirenade
sym 2207
1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol
abs 301
abs 302
abs 304
talampanel
talnetant
taltirelin
alpha amino 2,5 dihydro 5 oxo 4 isoxazolepropionic acid
tc 1734
tc 2559
tch 346
tgp 580
thurinex

CT Drug Descriptors:

tk 14
tp 20
traxoprodil
ts 011
21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione
2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol
ucm 3100
2 dipropylamino 5 methoxy 1 methyltetralin
uk 351666
uk 356464
uk 356297
v 2006
vp 025
vx 799
way 855
wib 63480 2
win 68100
win 69211
xaliprodene
y 931
ykp 1358
6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione
omega conotoxin MVIIA
zonampanel
zt 1
fluoratec
ladostigil
hypophysis adenylate cyclase activating polypeptide

RN (muscle relaxant agent) 9008-44-0; (calpastatin) 79079-11-1; (remacemide) 111686-79-4; (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (2

methyl 3 (2 pyrrolidinylmethoxy)pyridine) 161417-03-4; (6,7 dichloro 5 nitro 2,3 quinoxalinedione) 153504-81-5; (altropane) 127648-29-7; (donepezil) 120011-70-3, 120014-06-4, 142057-77-0; (asenapine) 85650-56-2; (aptiganel) 137159-92-3, 137160-11-3; (lanicemine) 153322-05-5; (bifeprunox) 350992-10-8; (2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 134296-40-5; (blonanserin) 132810-10-7; (alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol) 99931-60-9; (brasofensine) 171655-91-7, 171655-92-8, 173830-18-7, 173830-20-1; (cep 1347) 156177-65-0, 170587-65-2; (cep 751) 156177-59-2, 199280-60-9; (3 aminopropyl(diethoxymethyl)phosphinic acid) 123690-79-9; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (3,3 bis(3 fluorophenyl) n methylpropylamine) 186495-99-8; (10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone) 160588-45-4; (norphenazone) 89-25-8; (tsukubaenolide) 104987-11-3; (eliprodil) 119431-25-3, 127293-58-7, 136634-88-3; (pentoxifylline) 6493-05-6; (aloxistatin acid) 76684-89-4; (ascomycin) 104987-12-4; (n (4 acetyl 1 piperazinyl) 4 fluorobenzamide) 133920-70-4; (5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]) 133156-06-6; (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (ifenprodil) 23210-56-2; (ipenoxazone) 104454-71-9; (pralmorelin) 158861-67-7; (istradefylline) **155270-99-8**; (3 amino 1 hydroxy 4 methyl 2 pyrrolidinone) 130931-65-6; (5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid) 139051-78-8; (lamotrigine) 84057-84-1; (leteprinim) 138117-50-7, 192564-13-9; (5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone) 107889-32-7; (decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid) 136845-59-5; (decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid) 136109-04-1, 137433-06-8; (decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3 isoquinolinecarboxylic acid) 154652-83-2; (2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid) 176199-48-7; (4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine) 109348-38-1, 135991-48-9, 99487-25-9; (3 (2 carboxy 2 phenylethenyl) 4,6 dichloro 1h indole 2 carboxylic acid) 161230-88-2; (5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one) 116114-14-8; ([1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester) 88191-84-8; (3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid) 130798-51-5; (pramipexole) 104632-26-0; (2 (2 oxo 1 pyrrolidinyl) n (5,6,7,8 tetrahydro 2,3 dimethylfuro[2,3 b]quinolin 4 yl)acetamide) 135463-81-9; (lactacystin beta lactone) 154226-60-5; (icosapentaenoic acid ethyl ester) 73310-10-8; (2 [4 methoxy 3 (2 phenylethoxy)phenyl] n,n dipropylethylamine) 149409-57-4; (clomethiazole) 1867-58-9, 533-45-9; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (4 [(tert butylimino)methyl] 1,3 benzenedisulfonate disodium n oxide) 168021-79-2; (n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide) 103233-65-4; (2 dipropylamino 5,6 dimethoxyindan) 82668-33-5; (6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole) 172035-74-4; (7 dipropylamino 2,3,5,6,7,8 hexahydronaphtho[2,3 b]furan) 121454-18-0, 157622-55-4, 172549-26-7; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol) 191611-76-4; (3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate) 179120-52-6; (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4; (3 allyl 6 chloro 2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 80751-65-1; (7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone) 269718-83-4, 269718-84-5; (1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol) 142935-03-3; (talampanel) 161832-65-1, 161832-67-3; (talnetant)

174636-32-9, 204519-66-4; (taltirelin) 103300-74-9; (alpha amino 2,5 dihydro 5 oxo 4 isoxazolepropionic acid) 127607-88-9; (21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione) 110101-65-0; (2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol) 132535-61-6, 133681-84-2; (2 dipropylamino 5 methoxy 1 methyltetralin) 95999-11-4; (6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione) 143151-35-3, 154164-30-4; (omega conotoxin MVIIA) 107452-89-1; (hypophysis adenylate cyclase activating polypeptide) 137061-48-4

CN (1) Remacemide; (2) Selegiline; (3) Zydis; (4) 7b12; (5) Abt 089; (6) Abs 205; (7) A 72055; (8) A 366833; (9) A 35380; (10) A 134974; (11) Ac 184897; (12) Ac 90222; (13) Acea 1021; (14) Acp 103; (15) Acpc; (16) Ad gl0002; (17) Aeg 3482; (18) Aeol 10150; (19) Agy 110; (20) Agy 207; (21) Ak 275; (22) Vasolex; (23) Alaptid; (24) Ale 0540; (25) Altropane; (26) Am 36; (27) Aricept; (28) Ampakines; (29) An 1792; (30) Anatibant; (31) Apbpi 124; (32) Ar 139525; (33) Ar 15896; (34) Ar a 008055; (35) Ar r 17779; (36) Ar r 18565; (37) Arry 142886; (38) Arx 2000; (39) Arx 2001; (40) Arx 2002; (41) Asenapine; (42) Aptiganel; (43) As 600292; (44) Lanicemine; (45) As 004509; (46) As 601245; (47) Av 201; (48) Avp 923; (49) Axokine; (50) Az 36041; (51) Azd 0328; (52) Ba 1016; (53) Bay 38 7271; (54) Bay x 9227; (55) Bd 1054; (56) Besonprodil; (57) Bgc 20 1178; (58) Bia 3 202; (59) Bifeprunox; (60) Biii 890 cl; (61) Bimu 8; (62) Bls 602; (63) Blonanserin; (64) Bms 181100; (65) Brasofensine; (66) Breflate; (67) Bls 605; (68) Bts 72664; (69) Bvt 2989; (70) Bxt 51072; (71) Cdd 0304; (72) Cee 03 310; (73) Cee 03 320; (74) Cep 1347; (75) Cep 3122; (76) Cep 4186; (77) Cep 4186; (78) Cep 751; (79) Cere 20; (80) Cere 130; (81) Cere 120; (82) Cgp 35348; (83) Chf 2060; (84) Chf 3381; (85) Ckd 705; (86) Cnic 568; (87) Cns 2103; (88) Cns 5065; (89) Colostrinin; (90) Cp 132484; (91) Cp 283097; (92) Cp 465022; (93) Cpc 304; (94) Cx 516; (95) Dabelotine; (96) Dar 201; (97) DCG IV; (98) Dd 20207; (99) Nps 1506; (100) Delucemine; (101) Dmp 543; (102) Novasite; (103) Dp 103; (104) Dp 109; (105) Dp b99; (106) Dpp 225; (107) Dr 2313; (108) Dy 9760c; (109) E 2007; (110) E 2051; (111) E 2101; (112) Eaa 494; (113) Midafotel; (114) Eab 318; (115) Ect ad; (116) Ect pd; (117) Edaravone; (118) Ef 7412; (119) Egis 7444; (120) Eht 202; (121) Fk 506; (122) Eliprodil; (123) Eht 201; (124) Pentoxyfyllin; (125) Ep 475; (126) Eqa 00; (127) Anapsos; (128) Es 242 1; (129) F 10981; (130) F 2 ccg i; (131) Fce 29484a; (132) Fce 29642a; (133) Ersofermin; (134) Fk 520; (135) Fk 960; (136) Flindokalner; (137) Formobactin; (138) Fpl 16283; (139) Fr 210575; (140) Galdansetron; (141) Ganstigmine; (142) Liatermine; (143) Gke 841; (144) Glialines; (145) Throphix; (146) Gmc 1111; (147) Gp 14683; (148) Gpi 1485; (149) Gpi 1485; (150) Gr 1485; (151) Gr 73632; (152) Gt 2342; (153) Gt 715; (154) Gv 2400; (155) Gyki 52466; (156) Hf 0220; (157) Hp 184; (158) Ica 69673; (159) Idn 6556; (160) Ifenprodil; (161) Igt 440103; (162) Ino 1001; (163) Ipenoxazone; (164) Isp 1; (165) Clk 1; (166) It 657; (167) Kf 17329; (168) Kp 102; (169) Krp 199; (170) Krx 411; (171) Kw 6002; (172) L 687306; (173) L 687414; (174) L 689560; (175) L 701252; (176) Lamictal; (177) Lau 0501; (178) Lau 8080; (179) Lax 101; (180) Lentivector; (181) Leteprinim; (182) Liga 20; (183) Ly 178002; (184) Ly 233536; (185) Ly 274614; (186) Ly 293558; (187) Ly 302427; (188) Ly 354006; (189) Ly 354740; (190) Ly 451395; (191) Ly 483518; (192) M 40401; (193) Mcc 257; (194) Mci 225; (195) Mdl 100748; (196) Mdl 101002; (197) Mdl 102288; (198) Mdl 105519; (199) Mdl 27266; (200) Mdl 28170; (201) Mdl 29951; (202) Mecasermin; (203) Mem 1003; (204) Mem 1003; (205) Mirapex; (206) Mirapex; (207) Mito 4509; (208) Mito 4565; (209) Mkc 231; (210) Mln 519; (211) Mnd 21; (212) Ms 153; (213) Mt 5; (214) N 3393; (215) Nbi 30702; (216) Nc 531; (217) Ne 100; (218) Neotrofin; (219) Neramexane; (220) Neublastin; (221) Neurocale; (222) Neurostrol; (223) Neurovex; (224) Zendra; (225) Nla 715; (226) Nnc 07

0775; (227) Nnc 07 9202; (228) Noggin; (229) Norleu; (230) Nox 700
CN (231) Nps 1407; (232) Nps 846; (233) Nrt 115; (234) Ns 1209; (235) Ns 1608; (236) Ns 2330; (237) Ns 257; (238) Ns 377; (239) Ns 638; (240) Ns 649; (241) Nt 4; (242) Nt 5; (243) Nt 4; (244) Nt 5; (245) Nw 1048; (246) Nxd 5150; (247) Nxd 9062; (248) Nxy 059; (249) Nxy 059; (250) Ono 2506; (251) Opc 14117; (252) Org 24448; (253) P 58; (254) P 9939; (255) Pan 811; (256) Pbt 1; (257) Pd 132026; (258) Pd 148903; (259) Pd 150606; (260) Pd 159265; (261) Pd 90780; (262) Pdc 008 004; (263) Pe21; (264) Perzinfotel; (265) Pn 277; (266) Pn 401; (267) Pnu 87663; (268) Pnu 99194a; (269) Pnu 101033e; (270) Pnu 157678; (271) Pnu 170413; (272) Pnu 177864; (273) Pol 255; (274) Ppi 368; (275) Pre 103; (276) Prs 211220; (277) Pti 777; (278) Pym 50018; (279) Pym 50028; (280) Qg 2283; (281) Qr 333; (282) R 1485; (283) R 1577; (284) Ren 1654; (285) Ren 1820; (286) Rg 1068; (287) Ri 820; (288) Rjr 1401; (289) Rjr 2429; (290) Ro 09 2210; (291) Geomatrix; (292) Rpr 104632; (293) Rs 100642; (294) S 312 d; (295) S 1746; (296) S 14297; (297) S 14820; (298) S 176251; (299) S 34730 1; (300) S 34730; (301) S 18986; (302) S 33113 1; (303) S 33138; (304) Sarizotan; (305) Sb 203580; (306) Sb 271046; (307) Sb 277011; (308) Sca 136; (309) Sch 58261; (310) Sea 0400; (311) Semax; (312) Sib 1553a; (313) Sib 1765f; (314) Siclofen; (315) Sgs 518; (316) Sja 6017; (317) Skf 38393; (318) Skf 74652; (319) Skf 82958; (320) Sl 340026; (321) Sl 65 0155; (322) Slv 308; (323) Slv 314; (324) Slv 319; (325) Sm 13496; (326) SNX 482; (327) Sp (v5.2)c; (328) Spc 9766; (329) Sph 1371; (330) Spm 914; (331) Spm 935; (332) Sr 57667; (333) Sra 333; (334) Ssr 125047; (335) Ssr 146977; (336) Ssr 180575; (337) Ssr 181507; (338) Ssr 482073; (339) Ssr 504734; (340) Sumanirole; (341) Sun c5174; (342) Sun n8075; (343) Sun n8075; (344) Survivins; (345) Sirenade; (346) Sym 2207; (347) T 588; (348) Abs 301; (349) Abs 302; (350) Abs 304; (351) Talampanel; (352) Talampanel; (353) Talnetant; (354) Taltirelin; (355) Tan 950 a; (356) Tc 1734; (357) Tc 2559; (358) Tch 346; (359) Tgp 580; (360) Thurinex; (361) Tk 14; (362) Tp 20; (363) Traxoprodil; (364) Ts 011; (365) U 74500a; (366) U 78517f; (367) Ucm 3100; (368) Uh 232; (369) Uk 351666; (370) Uk 356464; (371) Uk 356297; (372) V 2006; (373) Vp 025; (374) Vx 799; (375) Vx 799; (376) Way 855; (377) Way 855; (378) Wib 63480 2; (379) Win 68100; (380) Win 69211; (381) Xaliprodene; (382) Y 931; (383) Ykp 1358; (384) Ym 90k; (385) Ziconotide; (386) Zonampanel; (387) Zt 1; (388) Ak 275; (389) Vasolex; (390) Fluoratec; (391) Ladostigil; (392) Liga 20; (393) PACAP; (394) Ampakines; (395) Ampakines; (396) Ampakines; (397) Apbpi 124

CO (3) Cardinal Health; (10) Abbott; (13) Cocensys novartis; (14) Acadia; (16) Actinodrug; (17) Aegera therapeutics; (18) Aeolus; (20) Agy therapeutics; (23) VUFB; (26) Amrad; (30) Fournier; (32) Arena; (37) Array biopharma; (40) Alpharx; (42) Oregon health sciences university; (47) Avigen; (48) Center for neurologic study; (50) Asahi Kasei; (52) Bioaxone; (55) Russian academy medical science; (56) Purdue neuroscience; (57) Sankyo; (58) Bial; (63) Dainippon; (66) Pharm eco; (67) Boston Life Sciences; (68) Knoll; (69) Biovitrum; (70) Oxis; (71) Cognitive; (77) Leo; (79) Stem cells

CO (80) The salk institute for biological studies; (81) University of washington; (85) Chong Kun Dang; (86) Cogent neuroscience; (88) CeNeS; (89) Regen; (93) Questcor; (96) Darpharma; (98) Diverdrugs; (100) NPS Pharmaceuticals; (105) D Pharm; (107) Meiji Seika Kaisha; (111) Eisai; (112) Btg novartis; (124) Exonhit therapeutics; (125) University of tennessee memphis; (127) Asac; (129) Fabre; (130) Tokyo metropolitan institute; (134) Kosan; (137) Kirin; (138) Fisons; (139) Fujisawa; (141) Chiesi; (142) Amgen; (143) Viatra viatris; (147) Sicor; (148) Guilford; (149) Symphony neuro development; (152) Gliatech; (153) GBtherapeutics; (154) BTG; (155) Egis; (156) Hunter Fleming; (158) Icagen; (159) Idun; (162) Inotek; (163) Nippon Chemiphar; (165) Chronogen; (166) Bristol Myers Squibb; (168) Krenitsky; (169) Kyorin; (170) Keryx; (171) Kyowa Hakko

Kogyo; (175) Merck and Co; (177) Louisiana university; (178) Louisiana state university; (179) Scotia holdings; (180) Oxford; (181) Spectrum; (182) Fidia; (192) Metaphore; (201) Hoechst Marion Roussel; (202) Cephalon; (203) Bayer; (204) Memory Pharmaceuticals; (206) Boehringer; (208) MitoKor; (210) PAION; (211) Mochida; (212) Mitsui; (214) Nisshin; (216) Neurochem; (218) NeoTherapeutics; (219) Merz; (220) Nsgene; (221) Apollo; (222) Neurocal; (223) Biovex; (227) Novo Nordisk; (228) Regeneron; (229) Hedral therapeutics; (230) Medinox; (232) Nps; (240) Neurosearch; (242) Genentech; (244) Ceregene; (245) Newron; (247) Nymox; (250) Ono; (251) Otsuka; (254) Aventis; (255) Panacea; (256) Prana Biotechnology; (261) Parke Davis; (262) Pharmaceutical Discovery; (263) Inserm; (265) Proneuron biotechnologies; (266) Wellstat Therapeutics; (272) Pharmacia; (273) Polifarma; (274) Praecis; (275) Prescient neuropharma; (276) Pharmos; (277) Proteotech; (279) Phytopharm; (280) Quark biotech; (281) Quigley; (284) Centaur; (285) Reneuron; (286) Repligen; (287) Rinat neuroscience; (289) Reynolds Tobacco; (292) Rhone Poulenc Rorer; (293) Hoffmann La Roche; (295) Shionogi; (303) Servier; (304) Merck AG; (311) Russian Academy of Sciences; (313) Sibia; (314) Schering Plough; (316) Senju; (318) Glaxo SmithKline; (320) Synthelabo; (324) Solvay; (325) Sumitomo

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CO Searle; Titan; Ryan; Nimh; Maas biolab; Pierre fabre reckitt and coleman; Purdue; Societe Misr Pour l'Industrie Pharmaceutique; Organix; Korea Research Institute; Juvantia; Oxford BioMedica; Glaxo Wellcome; Janssen; American Cyanamid; Curis; Tapestry; Acgera therapeutics; Ortho; Cytos Biotechnology; Ncrr; Yeda research; Research Triangle Institute; Renovis; Forest; Pharmed Private; Pharmacyclics; Sibia neuroscience; MERA; Toray; Tuszynski; Ucsd; Neurospheres; Beaufour; Johnson and Johnson; Lifegroup; Cellfactors; Alexion; University of nottingham; Richter; Teva; Asta; Aderis; Biofrontera; Sagami; Bresagen; Digital gene technologies; Novavax; Royal gist brocades; Us national institute on drug abuse; University of South Florida; University of pennsylvania; University of Georgetown; Samaritan; University of queensland; University of Oregon; Memorial sloan kettering cancer center; University of Chicago; Johns hopkins university; Hokkaido University; University of florence; Universita di sienna; University of kuopio; Finncovery

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ACCESSION NUMBER: 2004198619 EMBASE

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AUTHOR: Fischer F.; Matthisson M.; Herrling P.
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CT Medical Descriptors:
*degenerative disease: DT, drug therapy
Huntington chorea: DT, drug therapy
brain ischemia: DT, drug therapy
Parkinson disease: DT, drug therapy
epilepsy: DT, drug therapy
anxiety disorder: DT, drug therapy
schizophrenia: DT, drug therapy
pain: DT, drug therapy
Alzheimer disease: DT, drug therapy
spinal cord injury: DT, drug therapy
brain injury: DT, drug therapy
immune deficiency: DT, drug therapy
chronic obstructive lung disease: DT, drug therapy
enteritis: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
human
clinical trial
article
priority journal
Drug Descriptors:
remacemide: DV, drug development
remacemide: DT, drug therapy
remacemide: PD, pharmacology
selegiline: CT, clinical trial
selegiline: DT, drug therapy
selegiline: PD, pharmacology
adenosine kinase inhibitor: DV, drug development
adenosine kinase inhibitor: DT, drug therapy
adenosine kinase inhibitor: PD, pharmacology
nicotinic agent: DV, drug development
nicotinic agent: DT, drug therapy
nicotinic agent: PD, pharmacology
muscarinic agent: DV, drug development
muscarinic agent: DT, drug therapy
muscarinic agent: PD, pharmacology
nootropic agent: CT, clinical trial
nootropic agent: DT, drug therapy
nootropic agent: PD, pharmacology
calpastatin: DV, drug development
calpastatin: DT, drug therapy
calpastatin: PD, pharmacology
AMPA receptor antagonist: DV, drug development

AMPA receptor antagonist: DT, drug therapy
AMPA receptor antagonist: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DV, drug development
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
4 aminobutyric acid A receptor stimulating agent: DV, drug development
4 aminobutyric acid A receptor stimulating agent: DT, drug therapy
4 aminobutyric acid A receptor stimulating agent: PD, pharmacology
calcium channel blocking agent: DV, drug development
calcium channel blocking agent: DT, drug therapy
calcium channel blocking agent: PD, pharmacology
immunomodulating agent: CT, clinical trial
immunomodulating agent: DT, drug therapy
immunomodulating agent: PD, pharmacology
cholinesterase inhibitor: CT, clinical trial
cholinesterase inhibitor: DT, drug therapy
cholinesterase inhibitor: PD, pharmacology
serotonin agonist: DV, drug development
serotonin agonist: DT, drug therapy
serotonin agonist: PD, pharmacology
adrenergic receptor stimulating agent: DV, drug development
adrenergic receptor stimulating agent: DT, drug therapy
adrenergic receptor stimulating agent: PD, pharmacology
glutamate receptor agonist: DV, drug development
glutamate receptor agonist: DT, drug therapy
glutamate receptor agonist: PD, pharmacology
antioxidant: DV, drug development
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
alpha 2 adrenergic receptor blocking agent: CT, clinical trial
alpha 2 adrenergic receptor blocking agent: DT, drug therapy
alpha 2 adrenergic receptor blocking agent: PD, pharmacology
chelating agent: DV, drug development
chelating agent: DT, drug therapy
chelating agent: PD, pharmacology
serotonin 1A antagonist: CT, clinical trial
serotonin 1A antagonist: DT, drug therapy
serotonin 1A antagonist: PD, pharmacology
scavenger: DV, drug development
scavenger: DT, drug therapy
scavenger: PD, pharmacology
serotonin 3 antagonist: DV, drug development
serotonin 3 antagonist: DT, drug therapy
serotonin 3 antagonist: PD, pharmacology
glycine receptor antagonist: DV, drug development
glycine receptor antagonist: DT, drug therapy
glycine receptor antagonist: PD, pharmacology
potassium channel stimulating agent: CT, clinical trial
potassium channel stimulating agent: DT, drug therapy
potassium channel stimulating agent: PD, pharmacology
ionotropic receptor agonist: CT, clinical trial
ionotropic receptor agonist: DT, drug therapy
ionotropic receptor agonist: PD, pharmacology
caspase inhibitor: DV, drug development
caspase inhibitor: DT, drug therapy
caspase inhibitor: PD, pharmacology
muscarinic M1 receptor agonist: DV, drug development
muscarinic M1 receptor agonist: DT, drug therapy

muscarinic M1 receptor agonist: PD, pharmacology
monoamine oxidase B inhibitor: DV, drug development
monoamine oxidase B inhibitor: DT, drug therapy
monoamine oxidase B inhibitor: PD, pharmacology
cysteine proteinase inhibitor: DV, drug development
cysteine proteinase inhibitor: DT, drug therapy
cysteine proteinase inhibitor: PD, pharmacology
unindexed drug
a 134974
a 366833
a 35380
a 72055
abs 205
ac 184897
ac 90222
6,7 dichloro 5 nitro 2,3 quinoxalinedione
aeg 3482
CT Drug Descriptors:
agy 110
agy 207
ak 275
n (2 hydroxyethylamino) 3 nitronaphthalimide
am 36
Alzheimer disease vaccine
apbpi 124
ar 139525
ar 15896
ar a 008055
spiro[1 azabicyclo[2.2.2]octane 3,2' thiazolidine] 2' one
ar r18565
arry 142886
arx 2000
as 600292
as 004509
as 601245
az 36041
ba 1016
bay x 9227
bd 1054
bgc 20 1178
bls 602
bls 605
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide
alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol
cas 493
cep 1347
cep 4143
cep 3122
cep 4186
cep 751
cere 20
3 aminopropyl(diethoxymethyl)phosphinic acid
chf 2060
cnic 568
cns 1044
cns 2103
cns 5065
cp 132484

cp 283097
cpc 304
6 quinoxalinecarboxylic acid piperidide
2 (2,3 dicarboxycyclopropyl)glycine
dd 20207
10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone
dp 103
dp 109
dp b99
dpp 225
e 2101
eaa 404
eab 318
ef 7412
egis 7444
eht 202
aloxistatin acid
eqa 00
es 2421
f 10981
f 2 ccg 1
fce 29484 a
fibroblast growth factor 9
fpl 16283
ggf 2
gke 841
gp 14683
gpi 1337
gpi 1485
5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]
4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1
piperazinecarboxylic acid methyl ester
gt 2342
gt 715
gv 2400
1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine
hf 0220
hp 184
idn 6556
clk 1
isp 1
kf 17329
pralmorelin
krx 411
istradefylline
l 687306
3 amino 1 hydroxy 4 methyl 2 pyrrolidinone
5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic
acid
l 701252
lau 0501
liga 20
5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone
decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid
decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid
ly 302427
ly 354006
2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid
ly 451395

mcc 257
4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine
4 carboxymethylamino 5,7 dichloro 2 quinolinecarboxylic acid
3,4 dihydro 3,3 dimethylisoquinoline 2 oxide
mdl 102288
5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one
[1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester
3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid
mem 1003
lactacystin beta lactone
ms 153
mt 5
n 3393
nbi 30702
nc 531
5 (2 chloro 1 hydroxyethyl) 4 methylthiazole
nnc 070775
nnc 079202
nox 700

CT Drug Descriptors:

3 amino 1,1 bis(3 fluorophenyl)butane
nps 846
nrt 115
ns 1209
ns 1608
ns 257
ns 377
ns 638
ns 649
nxd 5150
nyx 059
ono 2506
n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide
p 58
p 9939
pan 811
pbt 1
pd 132026
pd 150606
pd 159265
pd 90780
pdc 008004
n sec butyl 1 (2 chlorophenyl) n methyl 3 isoquinolinecarboxamide
pn 277
6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole
pnu 157678
pnu 87663
pol 255
ppi 368
pre 368
prs 211220
pym 50028
qg 2283
ren 1654
ren 1820
ri 820

rjr 1401
ro 092210
rpr 104632
rs 100642
s 14820
s 176251
s 34730 1
s 18986
s 312 d
s 33113 1
5 chloro n [4 methoxy 3 (1 piperazinyl)phenyl] 3 methyl 2 benzothiophenesulfonamide
n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate
sja 6017
skf 74652
sl 340026
7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone
SNX 482
spc 9766
sph 1371
spm 914
spm 935
ssr 180575
ssr 482073
5 [3 [4 (4 fluorophenyl) 1 piperazinyl]propyl] 1,4,5,6,7,8 hexahydro 8 hydroxy 1 methylpyrrolo[3,2 c]azepin 4 one
sym 2207
1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol
abs 301
abs 302
abs 304
tan 950a
tc 2559
tch 346
tgp 580
tk 14
tp 20
21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione
2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol
uk 351666
uk 356464
uk 356297
vx 799
way 855
wib 63480 2
win 67500
win 68100
win 69211
6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione

RN (remacemide) 111686-79-4; (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (calpastatin) 79079-11-1; (6,7 dichloro 5 nitro 2,3 quinoxalinedione) 153504-81-5; (2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 134296-40-5; (alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol) 99931-60-9;

(cep 1347) 156177-65-0, 170587-65-2; (cep 751) 156177-59-2, 199280-60-9; (3 aminopropyl(diethoxymethyl)phosphinic acid) 123690-79-9; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone) 160588-45-4; (aloxistatin acid) 76684-89-4; (fibroblast growth factor 9) 151185-16-9; (5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]) 133156-06-6; (4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1 piperazinecarboxylic acid methyl ester) 126766-32-3; (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (pralmorelin) 158861-67-7; (istradefylline) **155270-99-8**; (3 amino 1 hydroxy 4 methyl 2 pyrrolidinone) 130931-65-6; (5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid) 139051-78-8; (5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone) 107889-32-7; (decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid) 136845-59-5; (decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid) 136109-04-1, 137433-06-8; (2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid) 176199-48-7; (4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine) 109348-38-1, 135991-48-9, 99487-25-9; (5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one) 116114-14-8; ([1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester) 88191-84-8; (3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid) 130798-51-5; (lactacystin beta lactone) 154226-60-5; (n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide) 103233-65-4; (n sec butyl 1 (2 chlorophenyl) n methyl 3 isoquinolinecarboxamide) 85532-75-8; (6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole) 172035-74-4; (4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol) 191611-76-4; (3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate) 179120-52-6; (7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone) 269718-83-4, 269718-84-5; (1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol) 142935-03-3; (21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione) 110101-65-0; (2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol) 132535-61-6, 133681-84-2; (6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione) 143151-35-3, 154164-30-4

CN (1) A 134974; (2) A 366833; (3) A 35380; (4) A 72055; (5) Abs 205; (6) Ac 184897; (7) Ac 90222; (8) Acea 1021; (9) Aeg 3482; (10) Agy 110; (11) Agy 207; (12) Ak 275; (13) Ak 275; (14) Ale 0540; (15) Am 36; (16) An 1792; (17) Apbpi 124; (18) Ar 139525; (19) Ar 15896; (20) Ar a 008055; (21) Ar r 17779; (22) Ar r18565; (23) Arry 142886; (24) Arx 2000; (25) As 600292; (26) As 004509; (27) As 601245; (28) Az 36041; (29) Ba 1016; (30) Bay x 9227; (31) Bd 1054; (32) Bgc 20 1178; (33) Bls 602; (34) Bls 605; (35) Bimu 8; (36) Bms 181100; (37) Cas 493; (38) Cep 1347; (39) Cep 4143; (40) Cep 3122; (41) Cep 4186; (42) Cep 751; (43) Cere 20; (44) Cgp 35348; (45) Chf 2060; (46) Cnic 568; (47) Cns 1044; (48) Cns 2103; (49) Cns 5065; (50) Cp 132484; (51) Cp 283097; (52) Cpc 304; (53) Cx 516; (54) DCG IV; (55) Dd 20207; (56) Dmp 543; (57) Dp 103; (58) Dp 109; (59) Dp b99; (60) Dpp 225; (61) E 2101; (62) Eaa 404; (63) Eab 318; (64) Ef 7412; (65) Egis 7444; (66) Eht 202; (67) Ep 475; (68) Eqa 00; (69) Es 2421; (70) F 10981; (71) F 2 ccg 1; (72) Fce 29484 a; (73) FGF 9; (74) Fpl 16283; (75) Ggf 2; (76) Gke 841; (77) Gp 14683; (78) Gpi 1337; (79) Gpi 1485; (80) Gr 73632; (81) Gr 89696; (82) Gt 2342; (83) Gt 715; (84) Gv 2400; (85) Gyki 52466; (86) Hf 0220; (87) Hp 184; (88) Idn 6556; (89) Clk 1; (90) Isp 1; (91) Kf 17329; (92) Kp 102; (93) Krx 411; (94) Kw 6002; (95) L 687306; (96) L 687414; (97) L 689560; (98) L 701252; (99) Lau 0501; (100) Liga 20; (101) Ly 178002; (102) Ly 233536; (103) Ly 235959; (104) Ly 274614; (105) Ly 302427; (106) Ly 354006; (107) Ly 354740; (108) Ly 451395; (109) Mcc 257; (110) Mci 225; (111) Mdl 100748; (112) Mdl 101002; (113) Mdl 102288; (114)

Mdl 27266; (115) Mdl 28170; (116) Mdl 29951; (117) Mem 1003; (118) Mln 519; (119) Ms 153; (120) Mt 5; (121) N 3393; (122) Nbi 30702; (123) Nc 531; (124) Nla 715; (125) Nnc 070775; (126) Nnc 079202; (127) Nox 700; (128) Nps 1407; (129) Nps 846; (130) Nrt 115; (131) Ns 1209; (132) Ns 1608; (133) Ns 257; (134) Ns 377; (135) Ns 638; (136) Ns 649; (137) Nxd 5150; (138) Nyx 059; (139) Ono 2506; (140) Opc 14117; (141) P 58; (142) P 9939; (143) Pan 811; (144) Pbt 1; (145) Pd 132026; (146) Pd 150606; (147) Pd 159265; (148) Pd 90780; (149) Pdc 008004; (150) Pk 11195; (151) Pn 277; (152) Pnu 101033e; (153) Pnu 157678; (154) Pnu 87663; (155) Pol 255; (156) Ppi 368; (157) Pre 368; (158) Prs 211220; (159) Pym 50028; (160) Qg 2283; (161) Ren 1654; (162) Ren 1820; (163) Ri 820; (164) Rjr 1401; (165) Ro 092210; (166) Rpr 104632; (167) Rs 100642; (168) S 14820; (169) S 176251; (170) S 34730 1; (171) S 18986; (172) S 312 d; (173) S 33113 1; (174) Sb 271046; (175) Sb 277011; (176) Sib 1553a; (177) Sib 1765f; (178) Sja 6017; (179) Skf 74652; (180) Sl 340026; (181) Slv 308; (182) SNX 482; (183) Spc 9766; (184) Sph 1371; (185) Spm 914; (186) Spm 935; (187) Ssr 180575; (188) Ssr 482073; (189) Sun c5174; (190) Sym 2207; (191) T 588; (192) Abs 301; (193) Abs 302; (194) Abs 304; (195) Tan 950a; (196) Tc 2559; (197) Tch 346; (198) Tgp 580; (199) Tk 14; (200) Tp 20; (201) U 74500a; (202) U 78517f; (203) Uk 351666; (204) Uk 356464; (205) Uk 356297; (206) Vx 799; (207) Way 855; (208) Wib 63480 2; (209) Win 67500; (210) Win 68100; (211) Win 69211; (212) Ym 90k

CO (4) Abbott; (7) Acadia; (8) Cocensys; (9) Aegera therapeutics; (11) Agy therapeutics; (13) Alkermes; (14) NPS Allelix; (15) Amrad; (17) Apollo

CO (18) Arena; (23) Array biopharma; (24) Alpharx; (28) Asahi Kasei; (29) Bioaxone therapeutique; (31) Russian academy of medical science; (32) Sankyo; (34) Boston Life Sciences; (35) Boehringer Ingelheim; (41) Leo; (42) Cephalon; (43) Stem cells; (45) Chiesi; (46) Cogent neuroscience; (52) Questcor; (53) Cortex; (55) Diverdrug; (56) Bristol Myers Squibb; (59) D Pharm; (61) Eisai; (63) Wyeth; (64) Universidad complutense de madrid; (66) Exonhit therapeutics; (67) University of tennessee memphis; (68) Asac; (70) Centre de reserche pierre fabre; (71) Tokyo metropolitan institute; (73) Amgen; (74) Fisons; (75) CeNeS; (76) Viatraviatris; (77) Sicor; (79) Guilford; (82) Gliatech; (83) GB; (84) BTG; (85) Egis; (86) Hunter Fleming; (88) Idun; (90) Chronogen; (92) Krenitsky; (93) Keryx; (94) Kyowa Hakko Kogyo; (98) Merck and Co; (99) Louisiana university; (100) Fidia; (108) Lilly; (110) Mitsubishi; (116) Hoechst Marion Roussel; (117) Bayer; (118) PAION; (119) Mitsui; (120) Taisho; (121) Nisshin; (122) Neurocrine bioscience; (123) Neurochem; (124) Astra Zeneca; (126) Novo Nordisk; (127) Medinox; (129) Nps; (136) Neurosearch; (137) Nymox; (139) Ono; (140) Otsuka; (142) Aventis; (143) Panacea; (144) Prana Biotechnology; (148) Parke Davis; (149) Pharmaceutical Discovery; (150) Universita di siena; (151) Proneuron biotechnologies; (155) Polifarma; (156) Praecis; (157) Prescient; (158) Pharmos; (159) Phytopharma; (160) Quark biotech; (161) Centaur; (162) Reneuron; (163) Rinat neuroscience; (164) Rj reynolds tobacco; (166) Rhone Poulenc Rorer; (167) Hoffmann La Roche; (172) Shionogi; (173) Servier; (177) Sibia; (178) Senju; (179) Glaxo SmithKline; (180) Synthelabo; (181) Solcvay; (182) Elan; (183) Celgene; (184) Sanochemia; (185) Alviva; (186) Albert ludwigs universitaet freiburg; (188) Sanofi Synthelabo; (189) Suntory; (190) Annovis; (191) Toyama; (194) American Biogenetic Sciences; (196) Targacept; (197) Novartis; (198) Takeda; (199) Lonza; (200) AVANT; (202) Pharmacia Upjohn; (205) Pfizer; (206) Serono; (207) Neurocrine Biosciences; (211) Sterling Winthrop; (212) Yamanouchi

CO Carlbiotech; Cardinal Health; University of South Florida; Fujimoto seiyaku; National Institute of Health; VUFB; University of California; Organon; Axonyx; Paracelsian; Immunogen; Oregon health sciences university; Pharmexa; Regeneron; Pharma eco; Ryan pharmaceuticals; Nimh; Maas biolab; Memorial sloankettering cancer center; Hebrew university;

Fabre; Schering; Societe Misr Pour l'Industrie Pharmaceutique; Korea research institute of bioscience and biotechnology; Knoll; National institute of aging; Searle; Kirin; Synaptica; Genentech; National institute of neurological disorders and stroke; American Cyanamid; Ncrr; Yeda research and development; Research Triangle Institute; Nippon Chemiphar; Spectrum; Merz; Pharmed Private; Pharmacyclics; MERA; Toray; NeoTherapeutics; Tuszynski; Nsgene; Neurocal; Hedral; Tulane University; Lifegroup; Inserm; Richter; Teva; Janssen; Newron; Russian Academy of Sciences; Schering Plough; Supratek; Ivax; Tanabe; Thuris; Us national institute drug abuse

L34 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610271 HCAPLUS
DOCUMENT NUMBER: 139:143978
TITLE: Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders
INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka; Ohsawa, Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063876	A2	20030807	WO 2003-US2658	20030128
WO 2003063876	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473864	AA	20030807	CA 2003-2473864	20030128
US 2004198753	A1	20041007	US 2003-353240	20030128
EP 1469855	A2	20041027	EP 2003-705971	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006919	A	20041109	BR 2003-6919	20030128
PRIORITY APPLN. INFO.:			US 2002-352413P P	20020128
			WO 2003-US2658 W	20030128

OTHER SOURCE(S): MARPAT 139:143978

AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e.,

L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

IC ICM A61K031-522
ICS A61P025-16

CC 1-11 (Pharmacology)

IT **Brain**
(substantia nigra, pars reticulata; adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

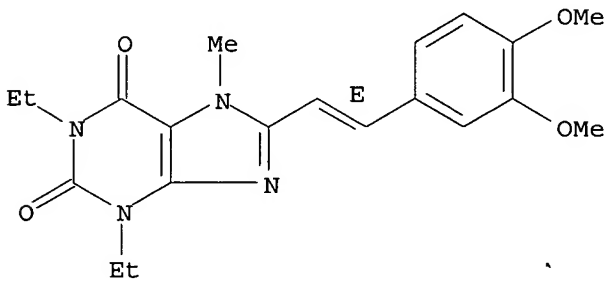
IT 69-89-6D, Xanthine, derivs. 322-35-0, Benserazide **155270-99-8**, KW 6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

IT **155270-99-8**, KW 6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376384 HCAPLUS

DOCUMENT NUMBER: 138:396214

TITLE: Methods and compositions for reducing ischemic injury of the heart by administering adenosine receptor agonists and antagonists

INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of U.S. 6,211,165.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003092668	A1	20030515	US 2001-800274		20010305
US 6586413	B2	20030701			
US 6211165	B1	20010403	US 1999-423129		19991105
PRIORITY APPLN. INFO.:			US 1999-423129	A2	19991105
			US 1997-46030P	P	19970509
			US 1997-61716P	P	19971010
			WO 1998-US9031	W	19980508

AB Compns. and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment of the invention comprises the simultaneous administration of specific A3/A1 receptor agonists to patients suffering from ischemic damage or at risk for the same. In yet another embodiment of the invention, a binary conjugate which acts as an agonist for the A3 receptor and an antagonist at the A2a receptor, is administered to reduce or prevent ischemic damage to the heart.

IC ICM A61K031-7076
INCL 514046000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63

IT **Anti-ischemic agents**
Apoptosis
Drug interactions
Human
Signal transduction, biological
Surgery
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

IT **Ischemia**
(cardiac; adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

IT 14114-46-6, DMPX 31377-34-1 **31377-36-3 31377-40-9**
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173845-91-5 173846-04-3, MRS 646 174365-19-6 193416-72-7
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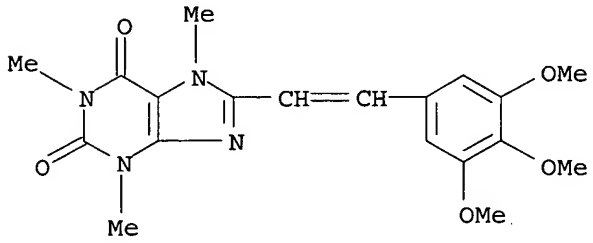
281191-59-1 312488-51-0, MRS 1543 524699-43-2 524699-44-3
528853-03-4, MRS 1525
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

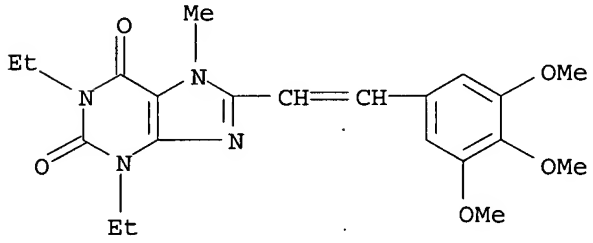
IT **31377-36-3 31377-40-9 149744-74-1**
158962-89-1 193416-91-0 193416-96-5
193416-97-6 212687-47-3 212687-48-4

212687-49-5 212687-50-8 212687-51-9
212687-52-0
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

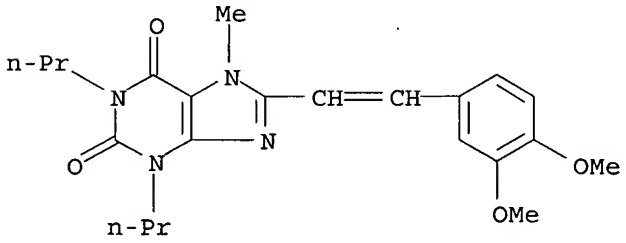
RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



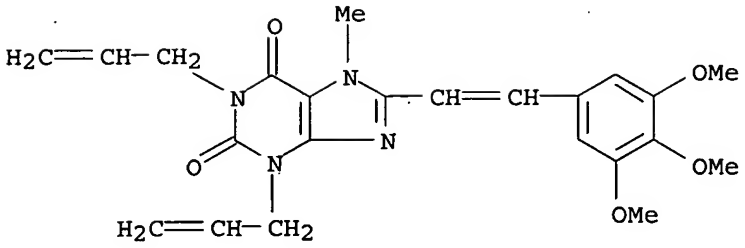
RN 31377-40-9 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



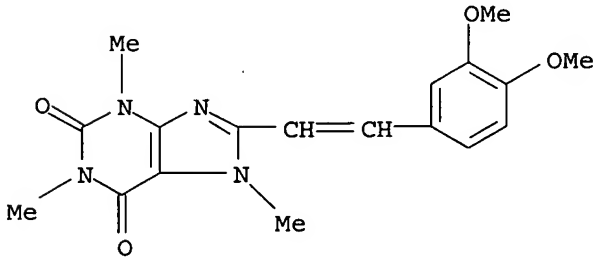
RN 149744-74-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)



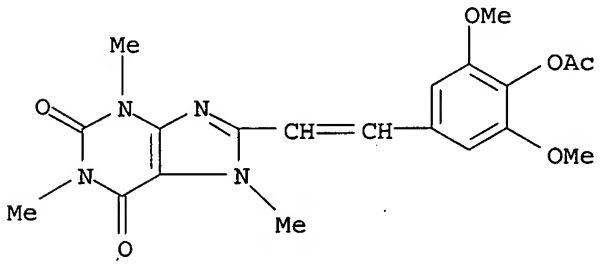
RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



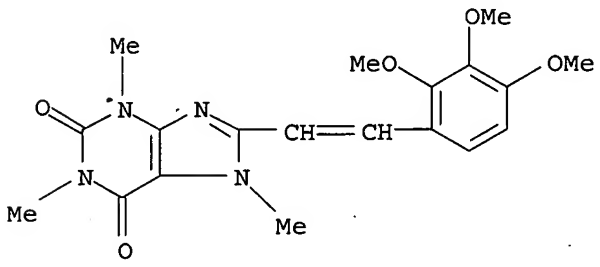
RN 193416-91-0 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



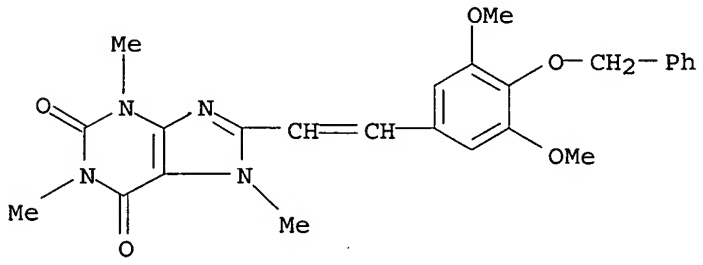
RN 193416-96-5 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



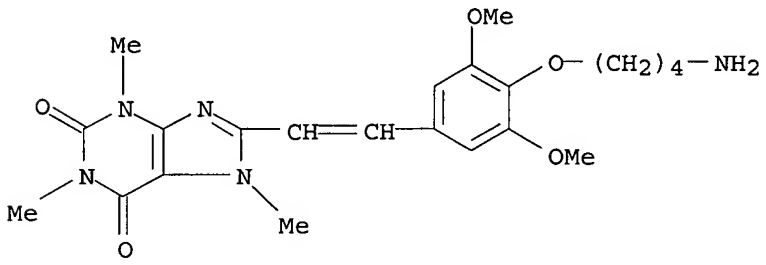
RN 193416-97-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



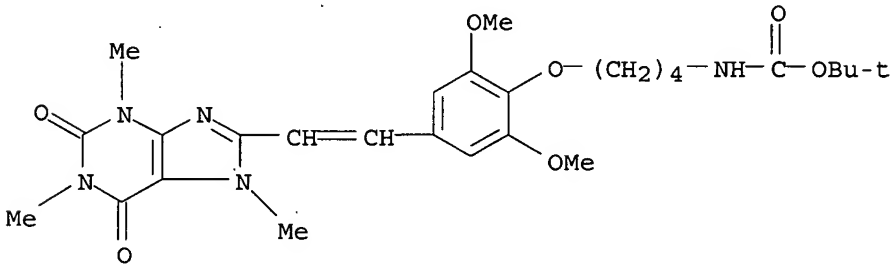
RN 212687-47-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 212687-48-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

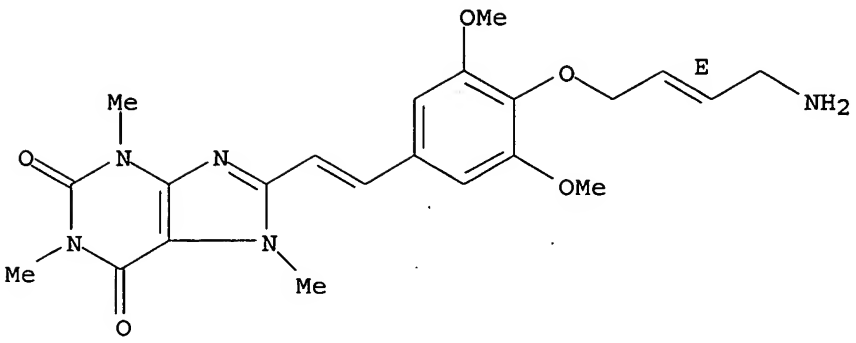


RN 212687-49-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



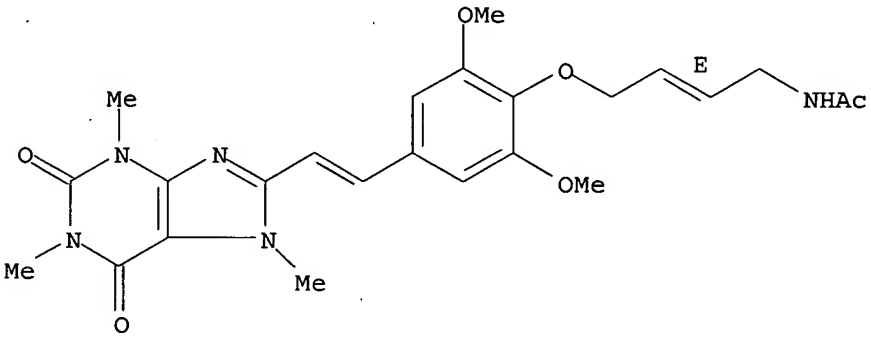
RN 212687-50-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



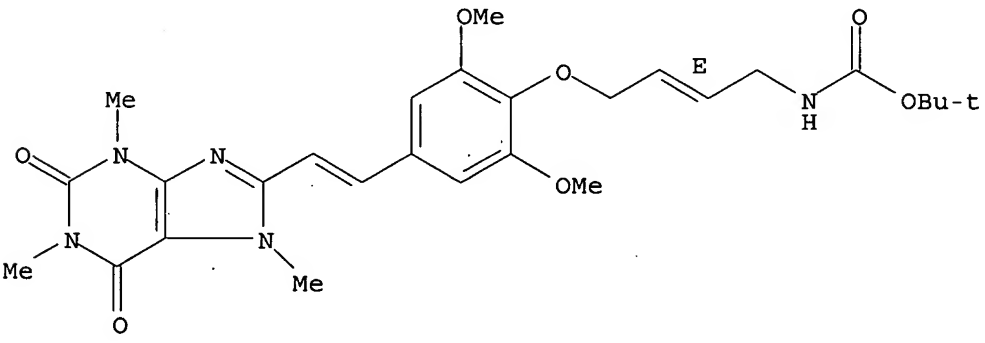
RN 212687-51-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



RN 212687-52-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



L34 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:978843 HCAPLUS

DOCUMENT NUMBER: 141:102286
TITLE: Potential of an adenosine A2A receptor antagonist [11C]TMSX for myocardial imaging by positron emission tomography: a first human study
AUTHOR(S): Ishiwata, Kiichi; Kawamura, Kazunori; Kimura, Yuichi; Oda, Keiichi; Ishii, Kenji
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Japan
SOURCE: Annals of Nuclear Medicine (2003), 17(6), 457-462
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous in vivo studies with mice, rats, cats and monkeys, we have demonstrated that [7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine ([11C]TMSX) is a potential radioligand for mapping adenosine A2A receptors of the **brain** by positron emission tomog. (PET). In the present study, we studied the potential of [11C]TMSX for myocardial imaging. Uptake of radioactivity by the heart was high and gradually decreased after an i.v. injection of [11C]TMSX into mice. In metabolite anal., 54% and 76% of the radioactivity in plasma and heart, resp., were present as the unchanged form of [11C]TMSX 60 min postinjection. The myocardial uptake was reduced by carrier-loading and by co-injection of an adenosine A2A antagonist CSC, but not by co-injection of an adenosine A1 antagonist DPCPX. Pretreatment with a high dose of a non-selective antagonist theophylline also reduced the myocardial uptake of [11C]TMSX. These findings demonstrate the specific binding of [11C]TMSX to adenosine A2A receptors in the heart. Finally we successfully performed the myocardial imaging by PET with [11C]TMSX in a normal volunteer. A graphical anal. by Logan plot supported the receptor-mediated uptake of [11C]TMSX. Peripherally [11C]TMSX was very stable in human: >90% of the radioactivity in plasma was detected as the unchanged form in a 60-min study. We concluded that [11C]TMSX PET has the potential for myocardial imaging.

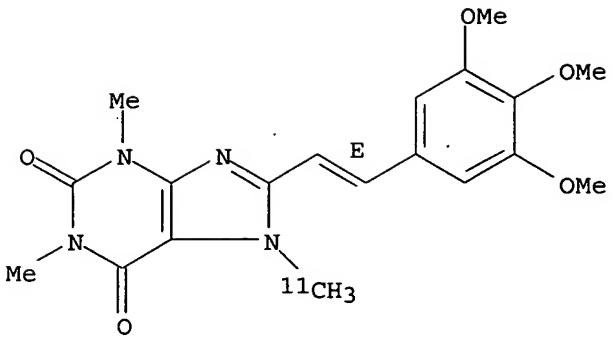
CC 8-9 (Radiation Biochemistry)

IT **223745-98-0**
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
(A2A receptor antagonist [11C]TMSX as PET agent for myocardial imaging)

IT **223745-98-0**
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
(A2A receptor antagonist [11C]TMSX as PET agent for myocardial imaging)

RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:677825 HCAPLUS
DOCUMENT NUMBER: 140:266862
TITLE: Preclinical studies on [11C]TMSX for mapping adenosine A2A receptors by positron emission tomography
AUTHOR(S): Ishiwata, Kiichi; Wang, Wei-Fang; Kimura, Yuichi; Kawamura, Kazunori; Ishii, Kenji
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Japan
SOURCE: Annals of Nuclear Medicine (2003), 17(3), 205-211
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous in vivo studies with mice, rats and monkeys, we have demonstrated that [11C]TMSX ([7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine) is a potential radioligand for mapping adenosine A2A receptors of the **brain** by positron emission tomog. (PET). In the present study, we performed a preclin. study. A suitable preparation method for [11C]TMSX injection was established. The radiation absorbed-dose by [11C]TMSX in humans estimated from the tissue distribution in mice was low enough for clin. use, and the acute toxicity and mutagenicity of TMSX were not found. The striatal uptake of [11C]TMSX in mice was reduced by pretreatment with theophylline at the dose of 10 and 100 mg/kg, suggesting that the [11C]TMSX PET should be carefully performed in the patients received with theophylline. We have concluded that [11C]TMSX is suitable for mapping adenosine A2A receptors in the human **brain** by PET.

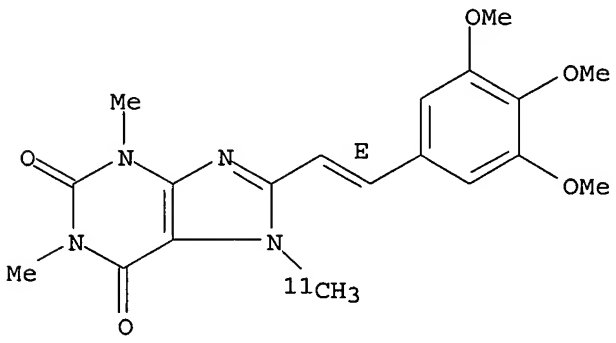
CC 8-9 (Radiation Biochemistry)
ST carbon 11 xanthine deriv adenosine receptor **brain** PET
IT **Brain**
Human
Positron-emission tomography
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)
IT **223745-98-0P**
RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); **PKT (Pharmacokinetics)**; PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)
IT **223745-98-0P**

RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); **PKT (Pharmacokinetics)**; PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)

RN 223745-98-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:904677 HCAPLUS

DOCUMENT NUMBER: 141:16533

TITLE: Translating A2A antagonist KW6002 from animal models to parkinsonian patients

AUTHOR(S): Chase, T. N.; Bibbiani, F.; Bara-Jimenez, W.; Dimitrova, T.; Oh-Lee, J. D.

CORPORATE SOURCE: National Institute of Neurological Disorders and Stroke, Experimental Therapeutics Branch, National Institutes of Health, Bethesda, MD, 20892-1406, USA

SOURCE: Neurology (2003), 61(11, Suppl. 6), S107-S111
CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Improving the translation of novel findings from basic laboratory research to better therapies for neurol. disease constitutes a major challenge for the neurosciences. This brief review of aspects of the development of an adenosine A2A antagonist for use in the management of Parkinson's disease (PD) illustrates approaches to some of the relevant issues. Adenosine A2A receptors, highly expressed on striatal medium spiny neurons, signal via kinases whose aberrant activation has been linked to the appearance of parkinsonian signs after dopaminergic denervation and to the motor response complications produced by dopaminomimetic therapy. To assess the ability of A2A receptor blockade to normalize certain of these kinases and thus benefit motor dysfunction, the palliative and prophylactic effects of the selective antagonist KW6002 were first evaluated in rodent and primate models. In hemiparkinsonian rats, KW6002 reversed the intermittent L-dopa treatment-induced, protein kinase A-mediated hyperphosphorylation of striatal α-amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid receptor GluR1 S845 residues and the

concomitant shortening in motor response duration. In 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned monkeys, coadministration of KW6002 with daily apomorphine injections acted prophylactically to prevent dyskinesia onset. These and related preclin. observations guided the design of a limited, randomized, controlled, proof-of-concept study of the A2A antagonist in patients with moderately advanced PD. Although KW6002 alone or in combination with a steady-state IV infusion of optimal-dose L-dopa had no effect on parkinsonian severity, the drug potentiated the antiparkinsonian response to low-dose L-dopa with fewer dyskinesias than produced by optimal-dose L-dopa alone. KW6002 also safely prolonged the efficacy half-time of L-dopa. The results suggest that drugs capable of selectively blocking adenosine A2A receptors could confer therapeutic benefit to L-dopa-treated parkinsonian patients and warrant further evaluation in phase II studies. They also illustrate a strategy for successfully bridging a novel approach to PD therapy from an evolving research concept to pivotal clin. trials.

CC 1-0 (Pharmacology)

IT **Brain**
(corpus striatum; translating A2A antagonist KW6002 from animal models to parkinsonian patients)

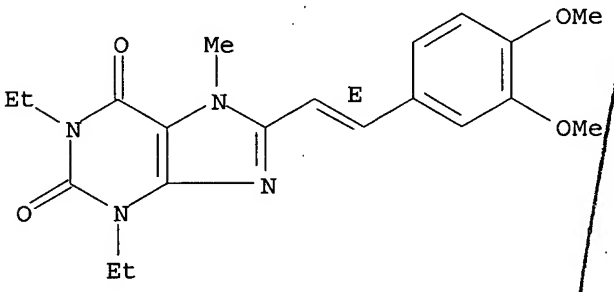
IT **155270-99-8**, KW6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(translating A2A antagonist KW6002 from animal models to parkinsonian patients)

IT **155270-99-8**, KW6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(translating A2A antagonist KW6002 from animal models to parkinsonian patients)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:793451 HCAPLUS
DOCUMENT NUMBER: 137:289033
TITLE: Adenosine A2A receptor antagonists combined with neurotrophic activity compounds in the treatment of Parkinson's disease

INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen, Karin Sandager
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002080957	A1	20021017	WO 2002-DK228		20020404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2440196	AA	20021017	CA 2002-2440196		20020404
EP 1379269	A1	20040114	EP 2002-759761		20020404
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004529916	T2	20040930	JP 2002-578996		20020404
US 2004097540	A1	20040520	US 2003-473809		20031002
PRIORITY APPLN. INFO.:			DK 2001-583	A	20010409
			WO 2002-DK228	W	20020404

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.

IC ICM A61K038-18
ICS A61K031-00; C07D473-04; C07K014-475; A61P025-16

CC 1-11 (Pharmacology)
Section cross-reference(s): 2

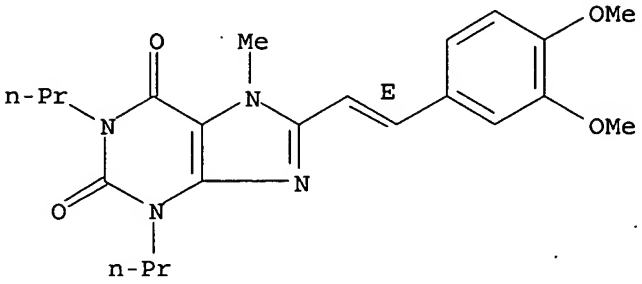
IT **Brain**
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT 14114-46-6, DMPX 104615-18-1, CGS-15943 139180-30-6, ZM-241385 **141807-96-7**, KF-17837 **155270-99-8**, KW-6002 160098-96-4, SCH-58261 160753-58-2 309711-72-6
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT **141807-96-7**, KF-17837 **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic compds.

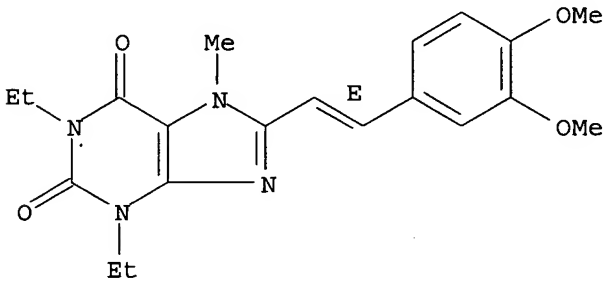
in treatment of Parkinson's disease)
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:90903 HCAPLUS
DOCUMENT NUMBER: 136:277364
TITLE: Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease
AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411-8731, Japan
SOURCE: Journal of Neurochemistry (2002), 80(2), 262-270
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the

present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

CC 14-10 (Mammalian Pathological Biochemistry)

IT **Brain**
(corpus striatum; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT **Brain**
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

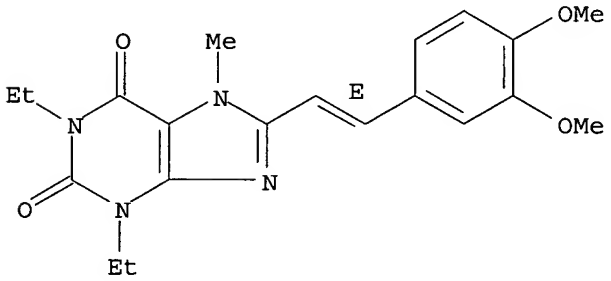
IT **155270-99-8**, KW-6002
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT **155270-99-8**, KW-6002
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 15 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002213683 EMBASE

TITLE: Adenosine as a neuroprotectant: Therapeutic perspectives.

AUTHOR: Phillis J.W.

CORPORATE SOURCE: Dr. J.W. Phillis, Department of Physiology, School of Medicine, Wayne State University, 540 E. Canfield Ave., Detroit, MI 48201, United States. jphillis@med.wayne.edu

SOURCE: Expert Review of Neurotherapeutics, (2002) Vol. 2, No. 2, pp. 167-176.
Refs: 81
ISSN: 1473-7175 CODEN: ERNXAR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020708
Last Updated on STN: 20020708

AB The potential for exploiting the neuroprotective properties of the purine nucleoside, adenosine, in a variety of CNS disorders, including: ischemic and traumatic injuries, neurodegenerative disorders, epilepsy and pain, has aroused considerable interest in both academic and pharmaceutical circles. A variety of approaches have been employed, ranging from the development of new selective agonists and antagonists for adenosine receptors, to compounds which can either potentiate extracellular levels of endogenously released adenosine or enhance its actions at receptors. Although many of these approaches were successful in animal studies, clinical trials have been delayed by the need to develop more potent and selective agents. With the recent promising advances in this area, future prospects for the development of new neurotherapeutic agents now appear promising.

CT Medical Descriptors:
*neuroprotection
brain ischemia
brain injury
degenerative disease
epilepsy
receptor intrinsic activity
human
review
Drug Descriptors:
*neuroprotective agent: DV, drug development
*neuroprotective agent: PD, pharmacology
*adenosine: DV, drug development
*adenosine: PD, pharmacology
purine nucleoside: DV, drug development
purine nucleoside: PD, pharmacology
adenosine receptor blocking agent: DV, drug development
adenosine receptor blocking agent: PD, pharmacology
adenosine receptor stimulating agent: DV, drug development
adenosine receptor stimulating agent: PD, pharmacology
adenosine A1 receptor agonist: DV, drug development
adenosine A1 receptor agonist: PD, pharmacology
adenosine A2a receptor agonist: DV, drug development
adenosine A2a receptor agonist: PD, pharmacology
adenosine A3 receptor agonist: DV, drug development
adenosine A3 receptor agonist: PD, pharmacology
adenosine A1 receptor antagonist: DV, drug development
adenosine A1 receptor antagonist: PD, pharmacology
adenosine A2 receptor antagonist: DV, drug development
adenosine A2 receptor antagonist: PD, pharmacology
adenosine A3 receptor antagonist: DV, drug development
adenosine A3 receptor antagonist: PD, pharmacology
cyclohexyladenosine: DV, drug development

cyclohexyladenosine: PD, pharmacology
6 n cyclopentyladenosine: DV, drug development
6 n cyclopentyladenosine: PD, pharmacology
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): DV, drug development
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): PD, pharmacology
6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine: DV, drug development
6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine: PD, pharmacology
8 cyclopentyltheophylline: DV, drug development
8 cyclopentyltheophylline: PD, pharmacology
8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine: DV, drug development
8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine: PD, pharmacology
4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol: DV, drug development
4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol: PD, pharmacology
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: DV, drug development
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: DV, drug development
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: PD, pharmacology
1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester: DV, drug development
1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester: PD, pharmacology
dipyridamole: DV, drug development
dipyridamole: PD, pharmacology
nitrobenzylthioinosine: DV, drug development
nitrobenzylthioinosine: PD, pharmacology
9 (2 hydroxy 3 nonyl)adenine: DV, drug development
9 (2 hydroxy 3 nonyl)adenine: PD, pharmacology
pentostatin: DV, drug development
pentostatin: PD, pharmacology
allopurinol: DV, drug development
allopurinol: PD, pharmacology
oxipurinol: DV, drug development
oxipurinol: PD, pharmacology
2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene: DV, drug development
2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene: PD, pharmacology
5 amino 4 imidazolecarboxamide riboside
unindexed drug

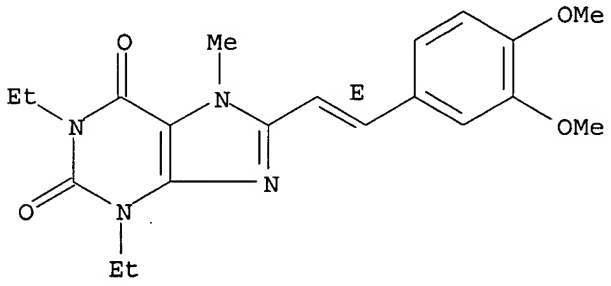
RN (adenosine) 58-61-7; (cyclohexyladenosine) 36396-99-3; (6 n cyclopentyladenosine) 41552-82-3; (2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide)) 120225-54-9; (6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine) 120442-40-2; (8 cyclopentyltheophylline) 35873-49-5; (8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine) 85872-51-1; (4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol) 139180-30-6; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine) **155270-99-8**; (1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester) 185222-90-6; (dipyridamole) 58-32-2; (nitrobenzylthioinosine) 65177-80-2;

(9 (2 hydroxy 3 nonyl)adenine) 59262-86-1; (pentostatin) 53910-25-1; (allopurinol) 315-30-0; (oxipurinol) 2465-59-0; (2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene) 132861-87-1; (5 amino 4 imidazolecarboxamide riboside) 2627-69-2

L34 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:787693 HCAPLUS
DOCUMENT NUMBER: 138:314421
TITLE: Distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in the rat **brain**
AUTHOR(S): Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa; Miyaji, Hiromasa; Sekine, Susumu; Kase, Hiroshi; Uchimura, Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Res. Inst., Kyowa Hakko Kogyo Co. Ltd., Sunto-gun, Shizuoka, 411-8731, Japan
SOURCE: Brain Research (2002), 953(1,2), 119-125
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [14C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [14C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the **brain**. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [14C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.
CC 1-11 (Pharmacology)
IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A, antagonist; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **Brain**
(corpus striatum; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT Antiparkinsonian agents
Parkinson's disease
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **Brain**
(forebrain; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)

IT Tachykinins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepro-; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT 93443-35-7, Preproenkephalin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **PKT (Pharmacokinetics)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **PKT (Pharmacokinetics)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001430941 EMBASE
TITLE: Adenosine A(2A) receptor antagonists: Potential therapeutic neuroprotective effects in parkinson's disease.
AUTHOR: Morelli M.; Wardas J.
CORPORATE SOURCE: J. Wardas, Department of Neuropsychopharmacol., Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland. micmor@tin.it
SOURCE: Neurotoxicity Research, (2001) Vol. 3, No. 6, pp. 545-556.
Refs: 87
ISSN: 1029-8428 CODEN: NURRFI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020103
Last Updated on STN: 20020103

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilisation of this drug. Recent experimental studies in which selective antagonists of adenosine A(2A) receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A(2A) antagonist [7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-(4,3-e)-1,2,4-triazolo(1,5--c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A(2A) receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-dietyl-8(3,4-dimethoxystyryl-7-methyl-3,7-dhydro-1H -purine-2,6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A(2A) receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An additional therapeutic potential of adenosine A(2A) antagonists emerged from studies showing neuroprotective properties of these compounds in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) (MPTP) model of PD. Adenosine A(2A) receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compounds for the treatment of PD.

CT Medical Descriptors:
*Parkinson disease: DT, drug therapy
drug activity
neuroprotection
drug efficacy
disease severity
psychosis: SI, side effect
dyskinesia: SI, side effect
long term care
drug utilization
motor dysfunction: DT, drug therapy
behavior
immunoreactivity
brain nerve cell
brain injury
corpus striatum
catalepsy: DT, drug therapy
primate
rigidity
disability
scoring system
marmoset
monkey
drug tolerance

brain ischemia: DT, drug therapy
brain ischemia: PC, prevention
neurotoxicity: DT, drug therapy
neurotoxicity: PC, prevention
nerve cell degeneration
human
nonhuman
mouse
rat
animal experiment
animal model
controlled study
article
priority journal
Drug Descriptors:
*5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
*adenosine receptor blocking agent: PD, pharmacology
levodopa: AE, adverse drug reaction
levodopa: DT, drug therapy
levodopa: PD, pharmacology
dopamine receptor stimulating agent
oxidopamine: PD, pharmacology
3,7 dimethyl 1 propargylxanthine: PD, pharmacology
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: DT, drug therapy
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: PD, pharmacology
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: DT, drug therapy
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: PD, pharmacology
haloperidol: TO, drug toxicity
reserpine: TO, drug toxicity
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: PK, pharmacokinetics
excitotoxin: TO, drug toxicity
bromocriptine
RN (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (levodopa) 59-92-7; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (3,7 dimethyl 1 propargylxanthine) 14114-46-6; (8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine) **141807-96-7** ; (8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine) **155270-99-8**; (haloperidol) 52-86-8; (reserpine) 50-55-5, 8001-95-4; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (bromocriptine) 25614-03-3

L34 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:811942 HCAPLUS
DOCUMENT NUMBER: 136:98481
TITLE: Evaluation of [4-O-methyl-11C]KW-6002 as a potential PET ligand for mapping central adenosine A2A receptors in rats
AUTHOR(S): Hirani, E.; Gillies, J.; Karasawa, A.; Shimada, J.; Kase, H.; Opacka-Juffry, J.; Osman, S.; Luthra, S. K.; Hume, S. P.; Brooks, D. J.
CORPORATE SOURCE: MRC Clinical Sciences Centre, Hammersmith Hospital, Imaging Research Solutions Ltd and PET Methodology Group, London, W12 0NN, UK
SOURCE: Synapse (New York, NY, United States) (2001), 42(3), 164-176
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB KW-6002, a xanthine-based adenosine A2A antagonist, was labeled with the positron emitter carbon-11 by O-methylation of its precursor, KF23325, using [11C]iodomethane and was evaluated in rats as a putative in vivo radioligand for positron emission tomog. (PET). Following i.v. injection of [11C]KW-6002, radioactivity was measured in blood, plasma, peripheral tissues, and in discrete **brain** tissues over a 2-h time period commensurate with PET scanning. In **brain**, [11C]KW-6002 showed highest retention in striata, with evidence of saturable binding, and lowest retention in frontal cortex (a tissue low in adenosine A2A receptors). PET scanning with [11C]KW-6002 demonstrated a specific signal in the striata which could be described using compartmental modeling. Specific binding was, however, also detected in extra-striatal regions, including **brain** areas reported to have low adenosine A2A receptor d. Blocking studies with the A1 selective antagonist KF15372 and the non xanthine-type A2A antagonist ZM 241385 failed to elucidate the nature of this binding. Thus, although [11C]KW-6002 shows some potential for development as a PET ligand for quantifying striatal adenosine A2A receptor function, its in vivo selectivity requires further investigation.

CC 8-9 (Radiation Biochemistry)

IT **Brain**
(corpus striatum, ligand distribution; [4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

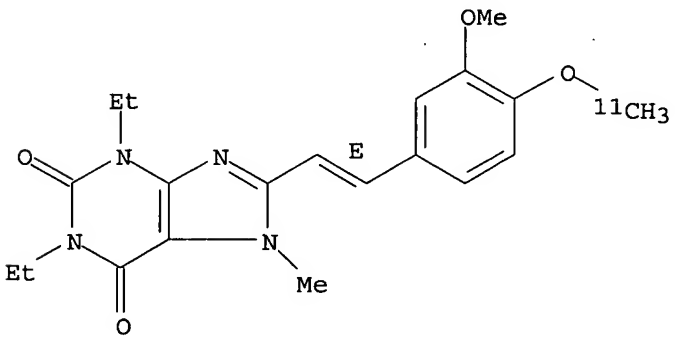
IT **389571-64-6**, [4-O-Methyl-11C]KW 6002
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
([4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

IT **389571-64-6**, [4-O-Methyl-11C]KW 6002
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
([4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

RN 389571-64-6 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-[3-methoxy-4-(methoxy-11C)phenyl]ethenyl]-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:135452 HCAPLUS

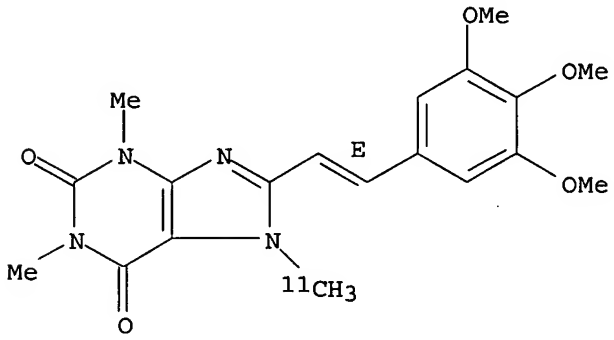
DOCUMENT NUMBER: 133:55385
TITLE: 11C-labeled KF18446: a potential central nervous system adenosine A2a receptor ligand
AUTHOR(S): Ishiwata, Kiichi; Noguchi, Junko; Wakabayashi, Shin-Ichi; Shimada, Junichi; Ogi, Nobuo; Nariai, Tadashi; Tanaka, Akira; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173-0022, Japan
SOURCE: Journal of Nuclear Medicine (2000), 41(2), 345-354
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To develop PET ligands for mapping central nervous system (CNS) adenosine A2a receptors that are localized in the striatum and are coupled with dopamine receptors, 3 11C-labeled xanthine-type adenosine A2a antagonists, [11C]KF18446 ([7-methyl-11C]-(E) -8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine), [11C]KF19631 ([7-methyl-11C]- (E)-1,3-diallyl-7-methyl-8- (3,4,5- trimethoxystyryl-)xanthine), and [11C]CSC ([7-methyl-11C] -8-chlorostyrylcaffeine), were compared with [11C]KF17837 ([7-methyl-11C]-(E)-8-(3,4-dimethoxystyryl) -1,3-dipropyl-7- methylxanthine). The regional **brain** uptake of the tracers, the effect of the coinjected adenosine antagonists on the uptake, and the metabolism were studied in mice. In rats, the regional **brain** uptake of the tracers was visualized by ex vivo autoradiog. (ARG). The A2a receptor binding of antagonist 1 was also measured by in vitro ARG. Imaging of the monkey **brain** was performed with PET with antagonist 1. In mice, the highest striatal uptake was found for antagonist 1 followed by antagonists 2 and 4. The uptake was inhibited by each of 3 KF compds. and by CSC, but not by an A1 antagonist KF15372. Another selective nonxanthine-type A2a antagonist SCH 58261 significantly decreased the striatal uptake of only antagonist 1, the labeled metabolites of which were less than 20% in the plasma 30 min postinjection, but were negligible in the **brain** tissue. In ex vivo ARG, antagonist 1 showed the highest striatal uptake and the highest uptake ratio of the striatum to the other **brain** regions. A high and selective binding of antagonist 1 to the striatum was also confirmed by in vitro ARG. PET with antagonist 1 visualized adenosine A2a receptors in the monkey striatum. These results indicate that antagonist 1 ([11C]KF18446) is the most suitable PET ligand for mapping adenosine A2a receptors in the CNS.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine A2a receptor carbon 11 KF18446
IT **Brain**
Positron-emission tomography
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
IT **223745-98-0**, [11C]KF 18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
IT **179678-39-8**, [11C]KF 17837 **278168-67-5**, [11C]KF 19631
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand: comparison with [11C]KF19631 and [11C]KF17837)

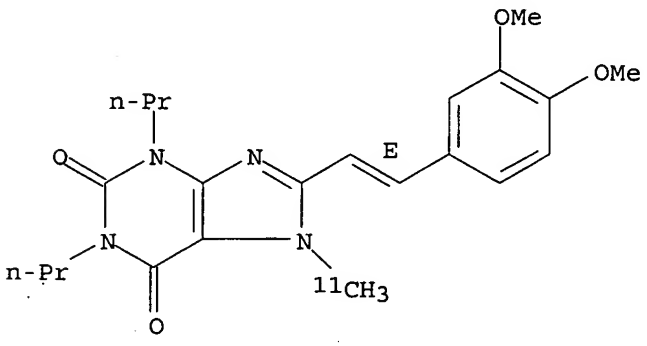
IT **223745-98-0**, [11C]KF 18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



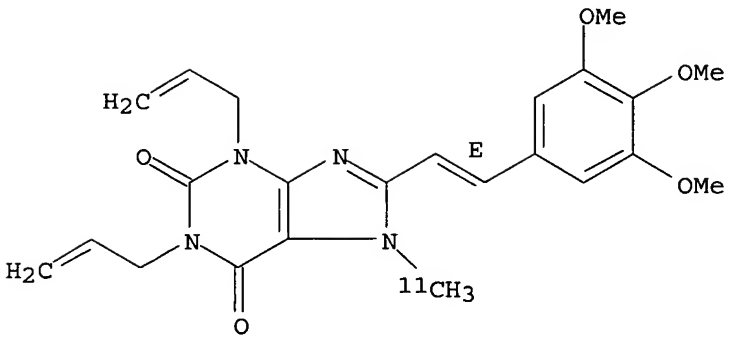
IT **179678-39-8**, [11C]KF 17837 **278168-67-5**, [11C]KF 19631
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand: comparison with [11C]KF19631 and [11C]KF17837)
RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 278168-67-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-(methyl-11C)-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:480897 HCAPLUS
DOCUMENT NUMBER: 133:346544
TITLE: Further characterization of a CNS adenosine A2a receptor ligand [11C]KF18446 with in vitro autoradiography and in vivo tissue uptake
AUTHOR(S): Ishiwata, Kiichi; Ogi, Nobuo; Shimada, Junichi; Nonaka, Hiromi; Tanaka, Akira; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173-0022, Japan
SOURCE: Annals of Nuclear Medicine (2000), 14(2), 81-89
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PET assessment of the adenosine A2a receptors localized in the striatum offers us a potential new diagnostic tool for neurol. disorders. In the present study, we carried out in vitro receptor autoradiog. of a newly developed PET ligand [11C]KF18446 ([7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine) with rat **brain** sections. [11C]KF18446 showed a high striatum/cortex binding ratio (5.0) and low nonspecific binding (<10%), suggesting that [11C]KF18446 has characteristics comparable or slightly superior to [3H]CGS 21680 or [3H]SCH 58261, which are currently available representative A2a receptor ligands. Scatchard anal. indicated a Kd of 9.8 nM and a Bmax of 170 fmol/mm3 tissue in the striatum and a Kd of 16.4 nM and a Bmax of 33 fmol/mm3 tissue in the cortex. Seven xanthine-type and four nonxanthine-type adenosine receptor ligands with an affinity for the adenosine A2a receptors significantly reduced the in vitro binding of [11C]KF18446 to the **brain** section. The blocking effects were much stronger in the striatum than in the cortex, but did not necessarily parallel their affinity. On the other hand, four xanthine-type ligands and one nonxanthine-type ligand (SCH 58261) of the 11 ligands studied reduced the in vivo uptake of [11C]KF18446 in mice, but other ligands, including A1-selective and nonselective ligands and three nonxanthine-type A2a-selective antagonists did not. We conclude that [11C]KF18446 is a promising adenosine A2a receptor ligand for PET study.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine receptor autoradiog carbon 11 KF18446
IT **Brain**
Positron-emission tomography

(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

IT **223745-98-0**, [11C]KF18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

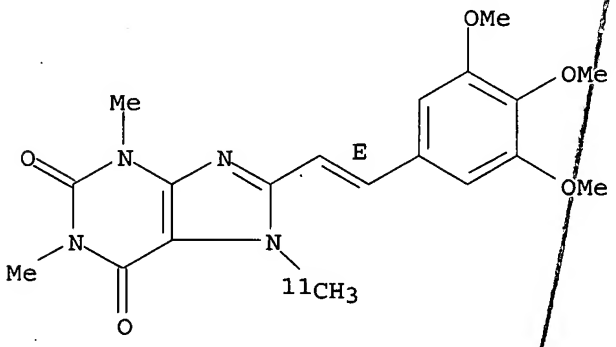
IT 120225-54-9, CGS 21680
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine agonist)

IT 14114-46-6, 3,7-Dimethyl-1-propargylxanthine **51389-37-8**, KF 18446 91896-57-0, CP 66713 96865-92-8, XAC 131080-42-7, KF 15372 139180-30-6, ZM 241385 **141807-96-7**, KF 17837 **142665-36-9**, KF 19631 147700-11-6, 8-(3-Chlorostyryl)caffeine 158747-27-4, ZD 9255 160098-96-4, SCH 58261
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine antagonists)

IT **223745-98-0**, [11C]KF18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

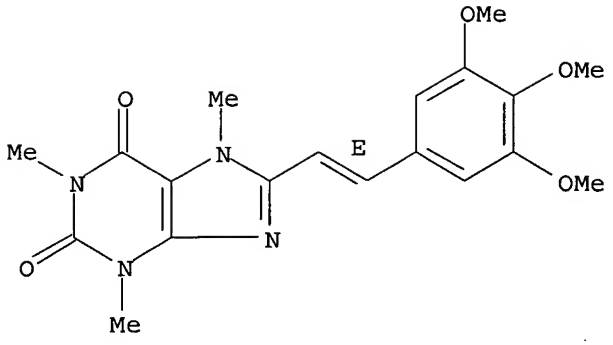
Double bond geometry as shown.



IT **51389-37-8**, KF 18446 **141807-96-7**, KF 17837 **142665-36-9**, KF 19631
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine antagonists)

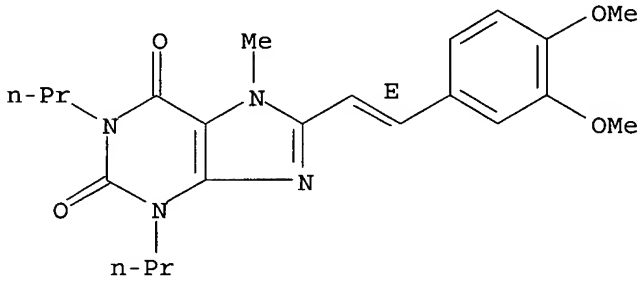
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



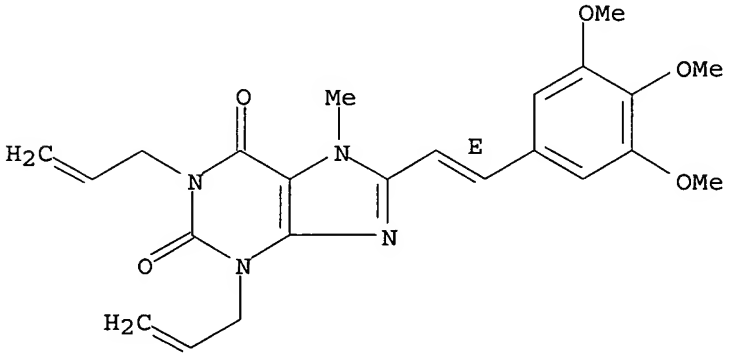
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:637359 HCAPLUS

DOCUMENT NUMBER: 134:430
TITLE: Systemic administration of adenosine A2A receptor antagonist reverses increased GABA release in the globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a microdialysis study
AUTHOR(S): Ochi, M.; Koga, K.; Kurokawa, M.; Kase, H.; Nakamura, J.; Kuwana, Y.
CORPORATE SOURCE: Kyowa Hakko Kogyo, Pharmaceutical Research Institute, Nagaizumi, Sunto, Shizuoka, 411-8731, Japan
SOURCE: Neuroscience (Oxford) (2000), 100(1), 53-62
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of adenosine A2A receptor antagonists to exhibit antiparkinsonian activity has recently been reported, but the mechanisms of action are still unknown. Since A2A receptors have been localized to GABAergic striatopallidal neurons, it is probable that these antagonists affect the activity of these neurons. In the present study, extracellular GABA basal levels were increased in the ipsilateral striatum and globus pallidus following a unilateral 6-hydroxydopamine lesion of the nigrostriatal pathway. The A2A receptor-selective antagonist KW-6002 (3 mg/kg, p.o.) caused a marked and sustained decrease of extracellular GABA levels in the globus pallidus of the 6-hydroxydopamine-lesioned rats, whereas no changes in GABA levels were observed in the globus pallidus of the non-lesioned rats. Microinjection of the A2A receptor agonist CGS21680 (0.005-0.5 μg) into the striatum of non-lesioned animals increased GABA concns. in the globus pallidus, which was abolished by the voltage-dependent Na+ channel blocker tetrodotoxin (1 μmol/l) delivered locally to the globus pallidus via the dialysis membrane. Furthermore, intrapallidal infusion of CGS21680 (10 μmol/l) also increased GABA levels in the globus pallidus. These data indicate that GABA release from striatopallidal neurons is regulated through A2A receptors in both the striatum and globus pallidus. The reversal of the 6-hydroxydopamine-induced increase in pallidal GABA levels by KW-6002 suggests that the antiparkinsonian effects of A2A receptor antagonists occur on the striatopallidal neurons.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 13, 14

IT **Brain**
(corpus striatum, GABAergic system; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **Brain**
(globus pallidus; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

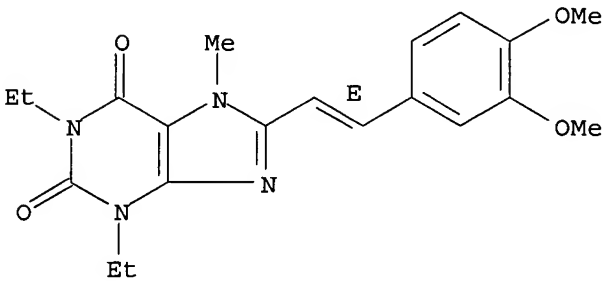
IT **Brain**
(striatopallidonigral tract; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **155270-99-8**, KW-6002
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **155270-99-8**, KW-6002
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:282105 HCAPLUS
DOCUMENT NUMBER: 130:306595
TITLE: Methods for reducing ischemic injury of the heart via the sequential administration of synergistic cardioprotective agents
INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA; National Institute of Health
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9920284	A1	19990429	WO 1998-US22515		19981023
W: AU, CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9913636	A1	19990510	AU 1999-13636		19981023
US 6329349	B1	20011211	US 2000-530164		20000424
PRIORITY APPLN. INFO.:			US 1997-62737P	P	19971023
			WO 1998-US22515	W	19981023

AB Materials and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment comprises methods of sequential administration of a plurality of cardioprotective agents (e.g. monophosphoryl lipid A and adenosine receptor agents).
IC ICM A61K031-715
ICS A61K031-44
CC 1-8 (Pharmacology)
Section cross-reference(s): 63

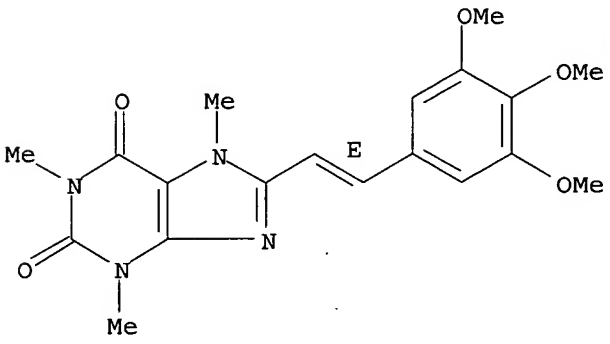
IT **Anti-ischemic agents**
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

IT 58-61-7, Adenosine, biological studies 16561-29-8, Phorbol 12-myristate 13-acetate 37739-05-2, 2-Chloro-N6-cyclopentyladenosine **51389-37-8** 60560-33-0, Pinacidil 65141-46-0, Nicorandil 96760-69-9 99765-13-6 103201-24-7 **141807-96-7** **142665-36-9** 147699-95-4 147699-98-7 147700-00-3 147700-02-5 147700-04-7 147700-05-8 147700-06-9 147700-07-0 147700-08-1 147700-10-5 147700-11-6 147700-13-8 **147700-19-4** 147700-20-7 147700-21-8 147700-23-0 147700-24-1 **147700-25-2** **147700-26-3** **147700-27-4** **147700-28-5** **147700-29-6** **147700-30-9** **147700-31-0** **147700-33-2** **147700-40-1** 147700-46-7 151539-31-0 152918-18-8 152918-28-0, MRS 1340 152918-39-3 163042-87-3, MRS 584 163152-33-8, MRS 537 163259-37-8, MRS 479 170966-25-3 173845-91-5 173846-04-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

IT **51389-37-8** **141807-96-7** **142665-36-9** **147700-19-4** **147700-25-2** **147700-26-3** **147700-27-4** **147700-28-5** **147700-29-6** **147700-30-9** **147700-31-0** **147700-33-2** **147700-40-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

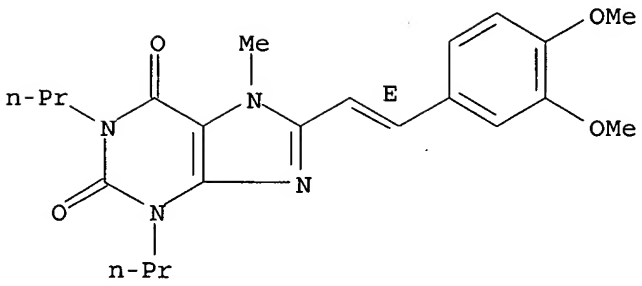
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



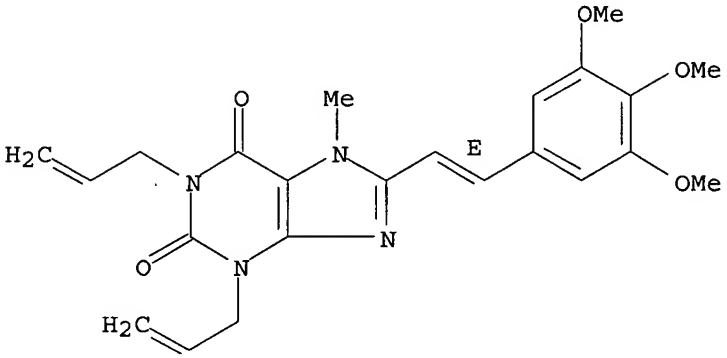
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



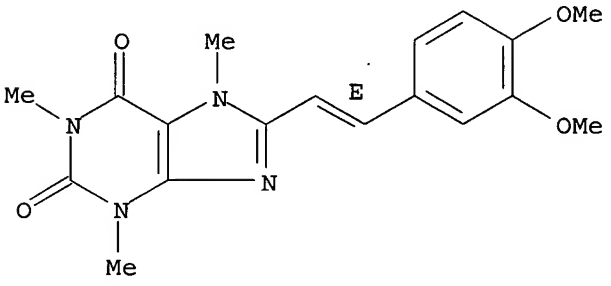
RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



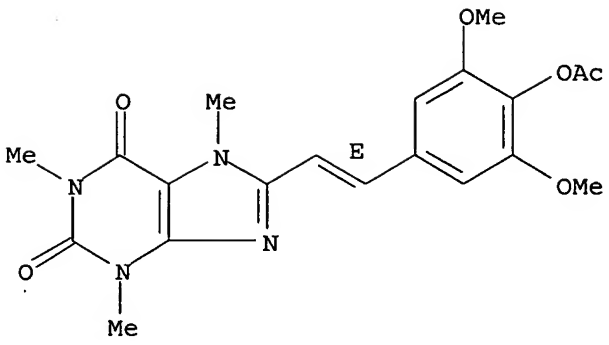
RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



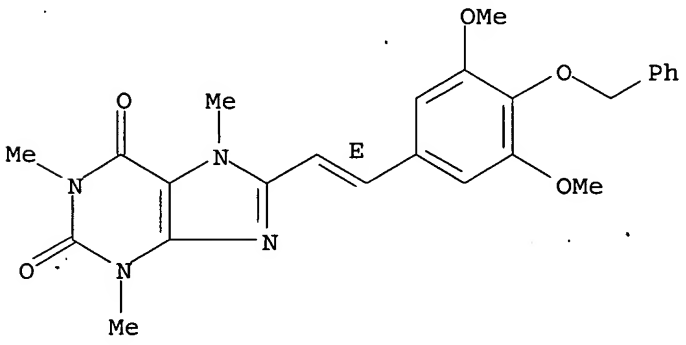
RN 147700-25-2 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



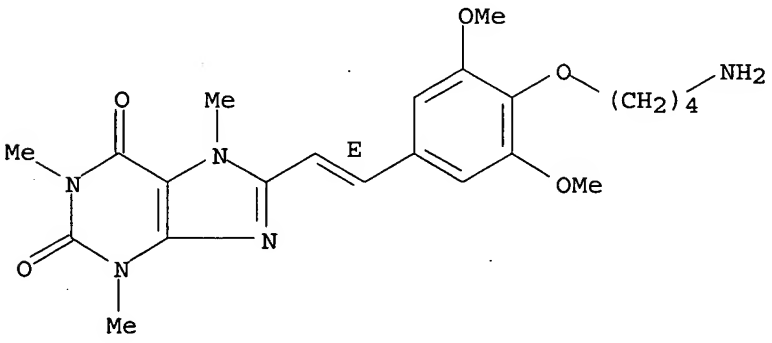
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

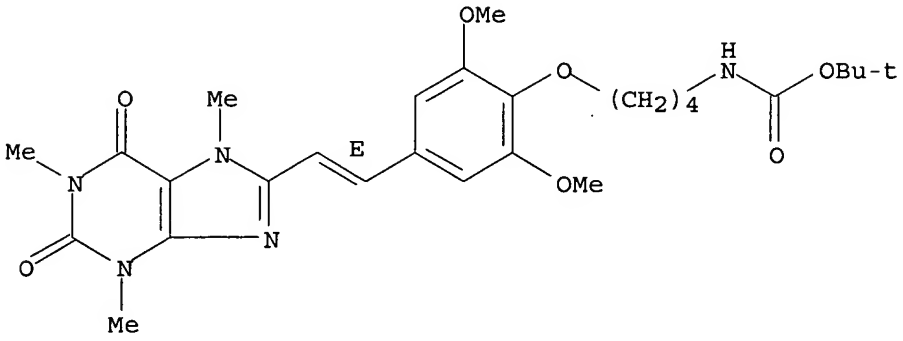
Double bond geometry as shown.



RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-,

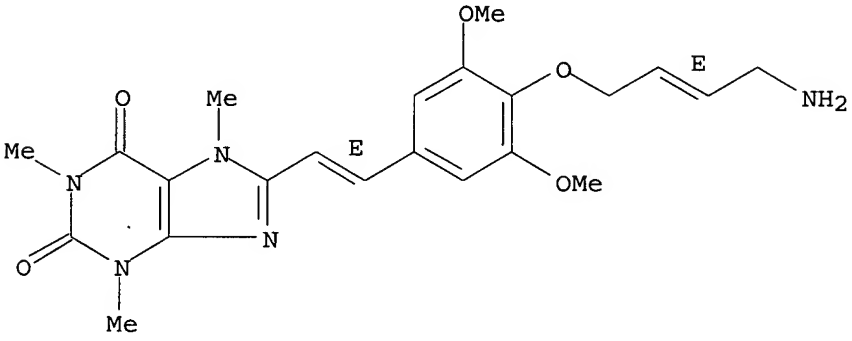
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



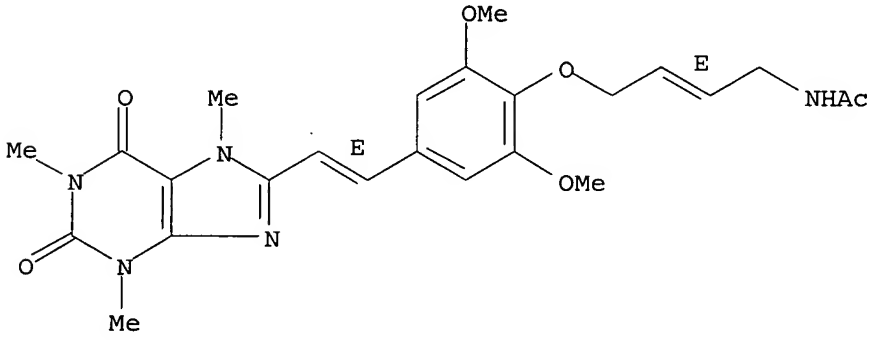
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



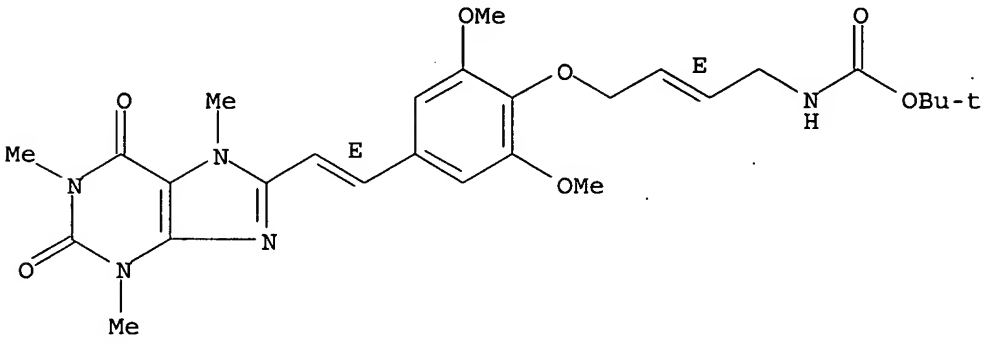
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



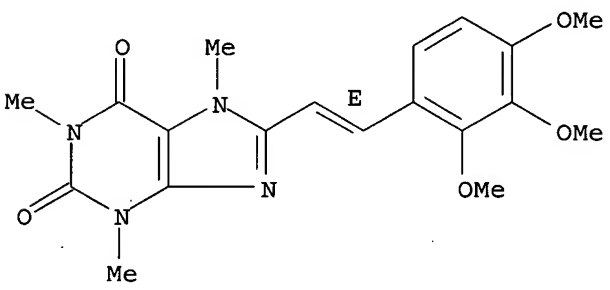
RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



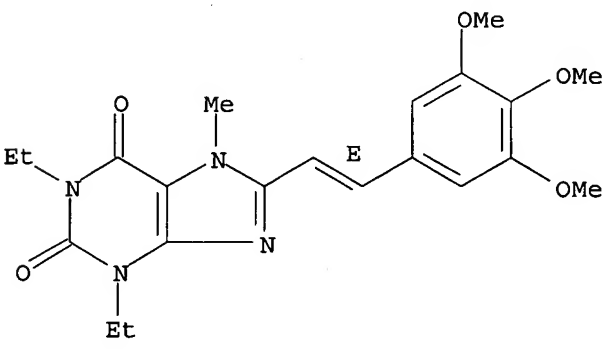
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

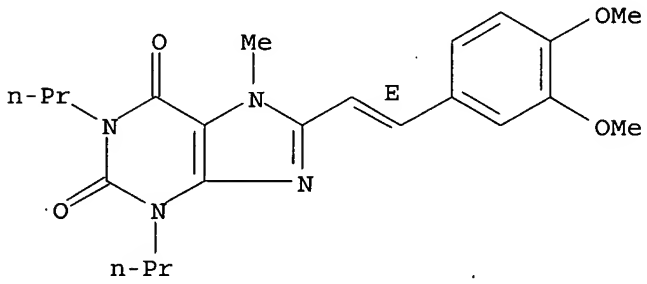
L34 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:693087 HCAPLUS
DOCUMENT NUMBER: 132:347
TITLE: Autoradiographic comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors
AUTHOR(S): Fredholm, Bertil B.; Lindstrom, Karin
CORPORATE SOURCE: Department of Physiology and Pharmacology, Section of Molecular Neuropharmacology, Karolinska Institutet, Stockholm, S-171 77, Swed.
SOURCE: European Journal of Pharmacology (1999), 380(2/3), 197-202
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have examined the potency of several adenosine receptor antagonists at adenosine A1 and A2A receptors using quant. autoradiog. and have compared the results with those of previous studies using the same radioligands in membrane prepns. The agonists [3H]cyclohexyladenosine and [3H]2-[p-(2-carbonylethyl)-phenylethylamino]-5'-N-ethylcarboxamido adenosine ([3H]CGS 21680) were used as radioligands for the two receptors. The results show that 1,3-dipropyl-8-cyclopentyl xanthine (DPCPX) is almost 1000-fold and 8-chloro-4-cyclohexyl-amino-1-(trifluoromethyl)[1,2,4]triazolo[4,3-a]quinoxaline (CP-68,247) about 300-fold more potent at adenosine A1 receptors in cortex and striatum than at striatal adenosine A2A receptors. Conversely, 5-amino-7-(2-phenylethyl)-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo [1,5-c]pyrimidine (SCH 58261) is approx. 1000-fold and 4-(2-[7-amino-2-(2-furyl)[1,2,4]-triazolo[2,3-a][1,3,5]triazin-5-yl amino]ethyl)phenol (ZM 241,385) about 400-fold more potent at adenosine A2A than at A1 receptors. Caffeine and its metabolites did not show any selectivity. Other studied antagonists were non-selective or showed a modest (20- to 40-fold) adenosine A2A receptor selectivity. Thus, only a few of the antagonists show such high selectivity that it is not offset by differences in drug distribution and levels of receptor subtype expression.

CC 1-11 (Pharmacology)
ST autoradiog adenosine receptor antagonist **brain**
IT **Brain**
(cerebral cortex; autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
IT **Brain**
(corpus striatum; autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 83-67-0, Theobromine 611-59-6, Paraxanthine 91895-50-0 91896-57-0, CP-66713 102146-07-6, 1,3-Dipropyl-8-cyclopentyl xanthine 104615-18-1, CGS 15943 127710-75-2, CP-68247 139180-30-6, ZM 241385 **141807-96-7**, KF 17837 147700-11-6 160098-96-4, SCH 58261
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A

receptors)
IT **141807-96-7**, KF 17837
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:334755 HCAPLUS
DOCUMENT NUMBER: 131:111326
TITLE: Effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice
AUTHOR(S): De Sarro, Giovambattista; De Sarro, Angela; Di Paola, Eugenio Donato; Bertorelli, Rosalia
CORPORATE SOURCE: Department of Experimental and Clinical Medicine, School of Medicine, University of Catanzaro, Catanzaro, 88100, Italy
SOURCE: European Journal of Pharmacology (1999), 371(2/3), 137-145
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have studied the effects of selective and non-selective adenosine receptor agonists and antagonists in audiogenic-seizure-sensitive DBA/2 mice, an animal model of generalized reflex epilepsy. With the exception of the adenosine A3 receptor agonist, N6-(3-iodobenzyl)-5'-N-methylcarboxamidoadenosine (IB-MECA), all the agonists studied prevented the development of audiogenic seizures in a dose-dependent manner. The ED50 values against the clonic phase of the audiogenic seizures were low, that is: 0.06 mg/kg, i.p., for the adenosine A1 receptor agonist, 2-chloro-N6-cyclopentyladenosine (CCPA), 0.02 and 0.03 mg/kg, i.p., for the adenosine A2A receptor agonists, 2-(4-(2-carboxyethyl)-phenylamino)-5'-N-ethylcarboxamidoadenosine (CGS 21680) and 2-hexynyl-5'-N-ethyl-carboxamidoadenosine (2-HE-NECA), and 0.7 mg/kg, i.p., for the adenosine Aj/A3 receptor agonist, N6-2-(4-aminophenyl)ethyladenosine (APNEA). Conversely, the non-selective agonist, N-ethyl-carboxamidoadenosine

(NECA), was highly potent, the ED50 being 0.0005 mg/kg, i.p. In the absence of auditory stimulation, the adenosine receptor antagonists increased the incidence of both clonic and tonic seizures in DBA/2 mice. The ED50 values were: for caffeine, 207.5 mg/kg, i.p., for the adenosine A, receptor antagonist, 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), 327.8 mg/kg i.p., for the adenosine A2A receptor antagonists, 3,7-dimethyl-1-propylxanthine (DPMX), 86.7 mg/kg i.p., for the (E,18%-Z,82%)7-methyl-8-(3,4-dimethoxystyryl)-1,3-dipropylxanthine (KF 17837), 69.1 mg/kg i.p., and 5-amino-7-(2-phenylethyl)-2-(2-furyl)-pyrazolo-(4,3-c)1,2,4-triazolo(1,5-c)-pyrimidine (SCH 58261), 321.8 mg/kg i.p. The rank order of convulsant potency in our epileptic model, following intracerebroventricular administration, was DPCPX > DMPX > 1,3,7-trimethyl-8-(3-chlorostyryl)xanthine (CSC) > KF 17837 > Caffeine > SCH 58261 > 5-amino-9-chloro-2-(2-furyl)-1,2,4-triazolo(1,5-c)quinazoline (CGS 15943). Following a subconvulsant audiogenic stimulus of 83 dB, all adenosine receptor antagonists induced both tonic and clonic seizures. The ED50 values for such proconvulsant effects were: for caffeine 0.04 mg/kg, i.p., for the adenosine A, receptor antagonist, DPCPX, 5.84 mg/kg, i.p., for the adenosine A2A receptor antagonists, DMPX, 0.02 mg/kg, i.p., CGS 15943, 0.29 mg/kg i.p., KF 17837, 0.57 mg/kg, i.p., CSC 0.12 mg/kg, i.p. and SCH 58261 0.07 mg/kg, i.p., resp. These data suggest that stimulation of adenosine A1 and A2A receptors is involved in the suppression of seizures.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 14

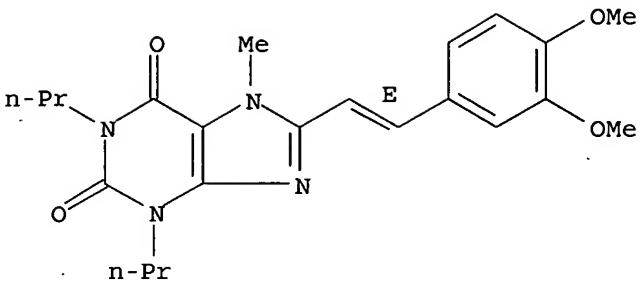
IT Anticonvulsants
Blood-**brain** barrier
Disease models
Epilepsy
Neurotransmission
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

IT 63906-63-8, 3,7-Dimethyl-1-propylxanthine 102146-07-6, DPCPX **141807-96-7**, KF 17837 148589-13-3 160098-96-4, SCH 58261
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

IT **141807-96-7**, KF 17837
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

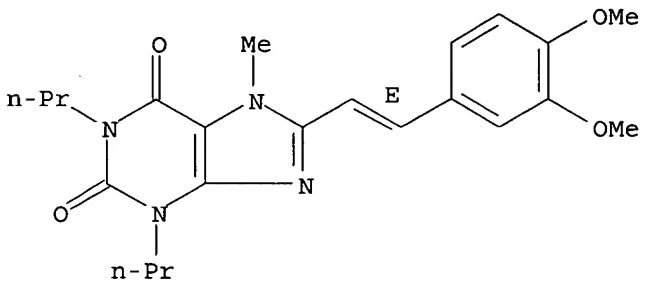


REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:713015 HCAPLUS
DOCUMENT NUMBER: 132:161113
TITLE: Effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice. [Erratum to document cited in CA131:111326]
AUTHOR(S): De Sarro, Giobambattista; De Sarro, Angela; Di Paola, Eugenio Donato; Bertorelli, Rosalia
CORPORATE SOURCE: Dep. Exp. and Clinical Med., Sch. Med., Univ. Catanzaro, Catanzaro, 88100, Italy
SOURCE: European Journal of Pharmacology (1999), 382(1), 51
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Table 3 has an error concerning the CD50 value of caffeine; the exact value is 192.8 (161.6-230.1).
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 14
ST erratum adenosine receptor agonist anticonvulsant epilepsy; adenosine receptor agonist anticonvulsant epilepsy erratum; receptor agonist anticonvulsant epilepsy model erratum; proconvulsant adenosine receptor antagonist epilepsy erratum; pharmacokinetic interaction anticonvulsant adenosine agonist erratum; blood **brain** barrier anticonvulsant adenosine agonist erratum; barrier anticonvulsant adenosine agonist epilepsy erratum
IT Anticonvulsants
Blood-**brain** barrier
Disease models
Epilepsy
Neurotransmission
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
IT 63906-63-8, 3,7-Dimethyl-1-propylxanthine 102146-07-6, DPCPX **141807-96-7**, KF 17837 148589-13-3 160098-96-4, SCH 58261
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
IT **141807-96-7**, KF 17837
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)

(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



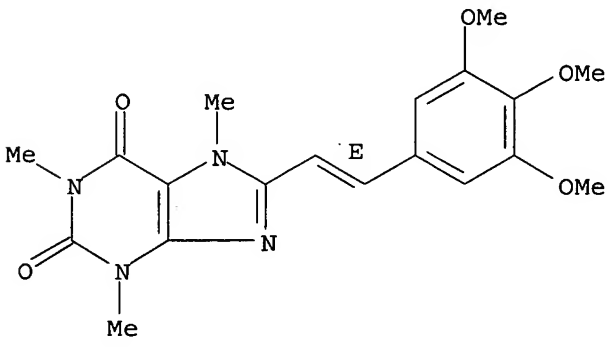
L34 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:744957 HCAPLUS
DOCUMENT NUMBER: 130:10632
TITLE: Methods and compositions for reducing ischemic injury of the heart by administering adenosine receptor agonists and antagonists
INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9850047	A1	19981112	WO 1998-US9031		19980508
W: AU, CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2289731	AA	19981112	CA 1998-2289731		19980508
AU 9873677	A1	19981127	AU 1998-73677		19980508
AU 750322	B2	20020718			
EP 991414	A1	20000412	EP 1998-920958		19980508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
US 6211165	B1	20010403	US 1999-423129		19991105
PRIORITY APPLN. INFO.:			US 1997-46030P	P	19970509
			US 1997-61716P	P	19971010
			WO 1998-US9031	W	19980508

AB Compns. and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment of the invention comprises the simultaneous administration of specific A3/A1 receptor agonists, to patients suffering from ischemic damage or at risk for the same. In yet another embodiment of the invention, a binary conjugate which acts as an agonist for the A3 receptor and an antagonist at the A2a receptor, is administered to reduce or prevent ischemic damage to the heart.

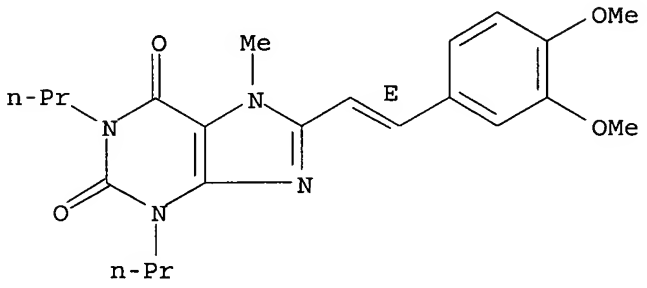
IC ICM A61K031-70
CC 1-8 (Pharmacology)
Section cross-reference(s): 33
IT **Anti-ischemic agents**
Protein sequences
Purinoceptor agonists
Purinoceptor antagonists
cDNA sequences
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
IT 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine 41552-82-3
51389-37-8 99765-13-6 103201-24-7 139180-30-6, ZM241385
141807-96-7 142665-36-9 147699-95-4 147699-98-7
147700-00-3 147700-02-5 147700-04-7 147700-05-8 147700-06-9
147700-07-0 147700-08-1 147700-10-5 147700-11-6 147700-13-8
147700-19-4 147700-20-7 147700-21-8 147700-23-0
147700-24-1 **147700-25-2 147700-26-3**
147700-27-4 147700-28-5 147700-29-6
147700-30-9 147700-31-0 147700-33-2
147700-40-1 147700-46-7 151539-31-0 152918-28-0
152918-39-3 160098-96-4, SCH58261 162684-35-7 163042-87-3
163152-33-8 163259-37-8 169190-74-3 170966-25-3 173845-91-5
173846-04-3 196497-15-1 199680-67-6 215933-83-8 215933-84-9
215933-88-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
IT **51389-37-8 141807-96-7 142665-36-9**
147700-19-4 147700-25-2 147700-26-3
147700-27-4 147700-28-5 147700-29-6
147700-30-9 147700-31-0 147700-33-2
147700-40-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



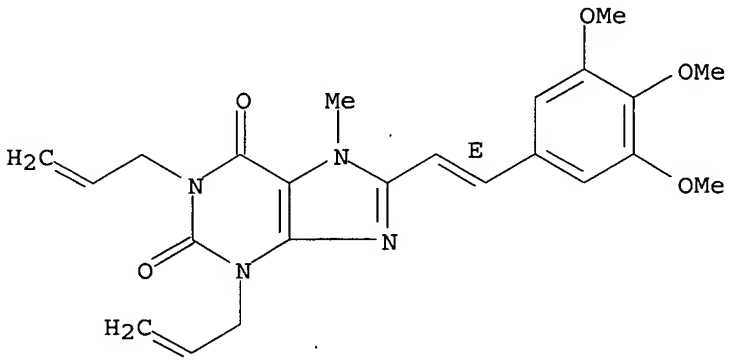
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



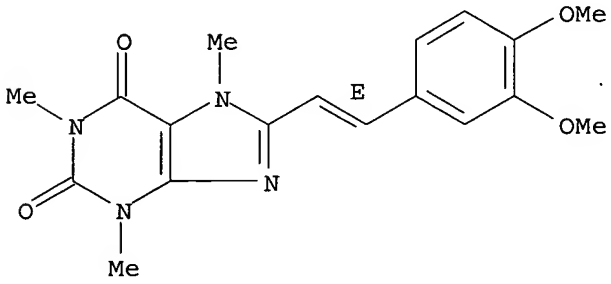
RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

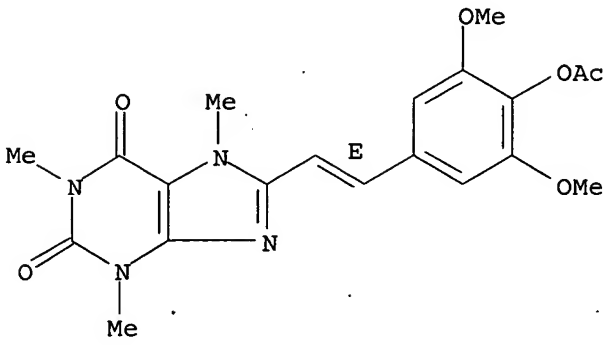
Double bond geometry as shown.



RN 147700-25-2 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-

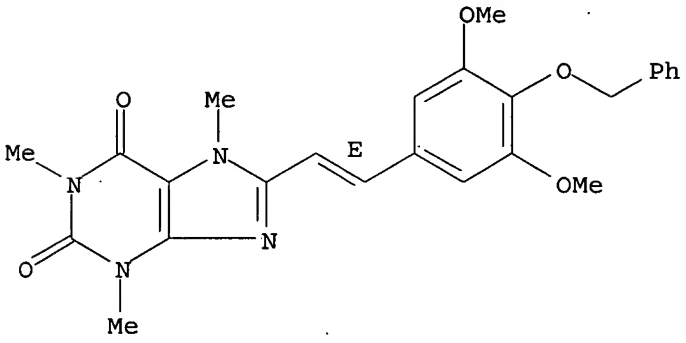
3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



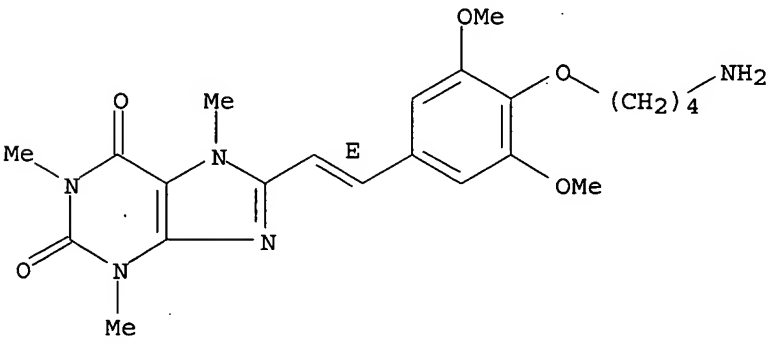
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



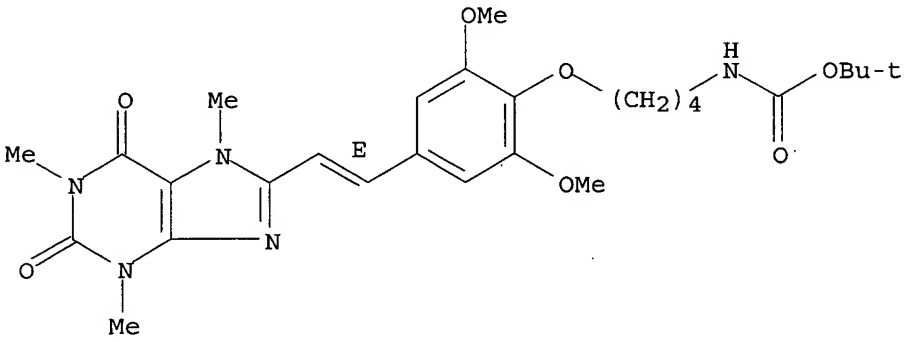
RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



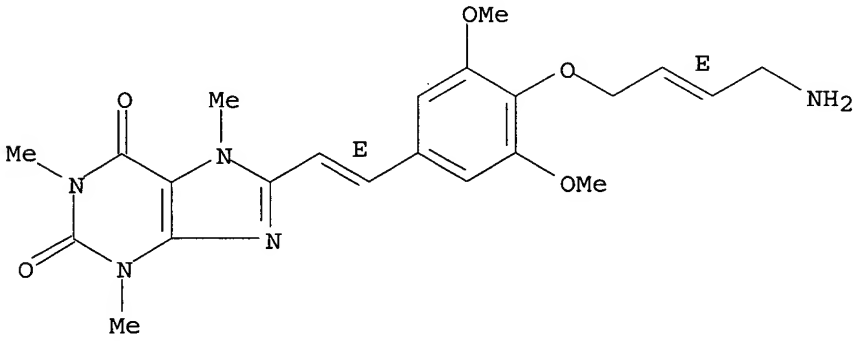
RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



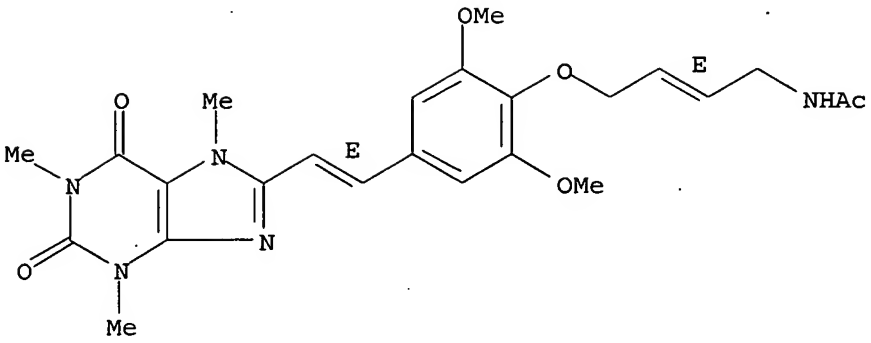
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



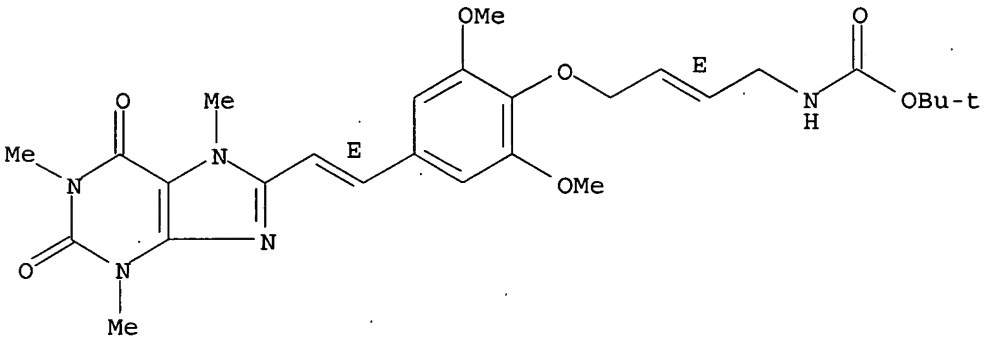
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



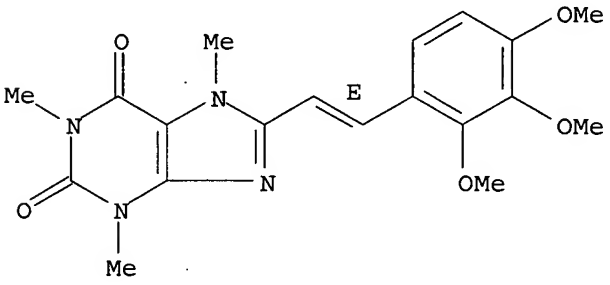
RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



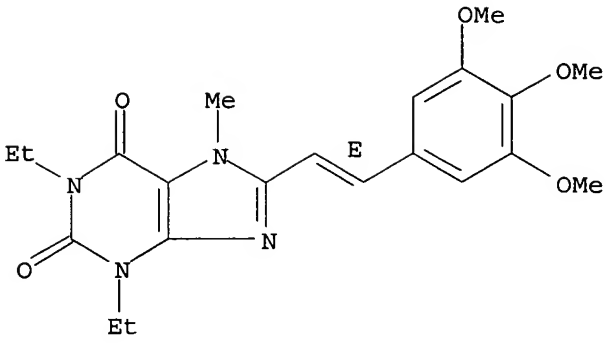
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:644563 HCAPLUS
DOCUMENT NUMBER: 130:33316
TITLE: Adenosine A2A receptors modify motor function in MPTP-treated common marmosets
AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana, Yoshihisa; Jenner, Peter
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co Ltd, Shizuoka, 411-8731, Japan
SOURCE: NeuroReport (1998), 9(12), 2857-2860
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both adenosine A1 and A2 receptor populations are located in the striatum and can modify locomotor activity, and they may form a therapeutic target for Parkinson's disease (PD). Administration of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione (KW-6002) to MPTP-treated common marmosets increased locomotor activity. In contrast, administration of the selective A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxantine (DPCPX) had no effect on locomotion. Administration of the adenosine A2A receptor agonist 2-[p-[2-(2-aminoethylamino) carbonylethyl] phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose dependently suppressed basal locomotor activity. A minimally ED of APEC (0.62 mg/kg, i.p) completely reversed the increase in locomotor activity produced by administration of KW-6002. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1, 14

IT **Brain**, disease
(basal ganglion; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT **Brain**
(corpus striatum; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT **155270-99-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptors modify motor function in MPTP-treated common

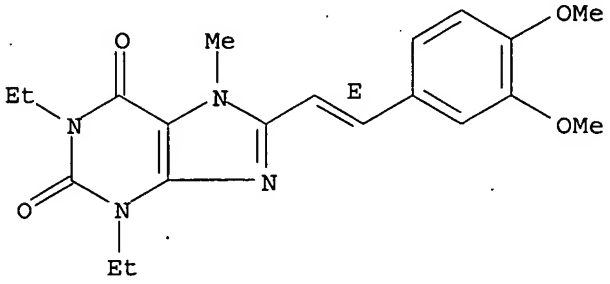
marmoset Parkinsonism model)

IT **155270-99-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:394679 HCAPLUS

DOCUMENT NUMBER: 129:118143

TITLE: Pharmacological characterization of a simple behavioral response mediated selectively by central adenosine A1 receptors, using in vivo and in vitro techniques

AUTHOR(S): Marston, Hugh M.; Finlayson, Keith; Maemoto, Takuya; Olverman, Henry J.; Akahane, Atsushi; Sharkey, John; Butcher, Steven P.

CORPORATE SOURCE: Fujisawa Institute of Neuroscience, University of Edinburgh, Edinburgh, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(3), 1023-1030
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The behavioral profile of a range of adenosine receptor ligands was examined in rats using a locomotor activity model. Adenosine receptor agonists, including the selective A1 receptor agonist, N6-cyclopentyladenosine (CPA) and the A2A agonist, 2-[(2-aminoethylamino)carbonylethyl-phenylethylamino]-5'- ethylcarboxamidoadenosine (APEC), reduced spontaneous motor activity in a dose-dependent manner. CPA-induced locomotor depression was attenuated by adenosine A1 receptor selective antagonists, such as 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-2-piperidine ethanol (FK453), and (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-piperidin-2-yl acetic acid (FK352), but not by the A2A receptor antagonist, (E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine (KF17837). By contrast, APEC-induced hypolocomotion was attenuated by KF17837 but not by

DPCPX, confirming that adenosine A1 and A2A receptor activation mediates locomotor output independently. Two peripheral adenosine receptor antagonists, 8-(p-sulfophenyl)-1,3-dipropylxanthine (DPSPX) and 8-(p-sulfophenyl)-1,3-dimethylxanthine (8-PST), did not alter CPA-induced hypolocomotion. This confirmed that pharmacol. reversal of the adenosine A1 receptor-mediated response involved a central site of drug action. The relationship between occupancy of central adenosine A1 receptors and behavioral effect was therefore assessed. Regression anal. on log transformed data confirmed assocns. between antagonist affinity for **brain** [3H]DPCPX binding sites and, in order of increasing significance, the equivalent behavioral dose (EBD) for reversal of CPA-induced hypolocomotion (R2 = 0.32), the serum concentration of drug (R2 = 0.65), and most significantly with the **brain** concentration of drug detected 20 min after administration of the (EBD) (R2 = 0.95). These data suggest that competition between agonists and antagonists, for occupancy of central adenosine A1 receptors, is intrinsic to the pharmacol. reversal of CPA-induced hypolocomotion. The validity of the model as a simple predictive screen for the blood/**brain** barrier permeability of adenosine A1 receptor antagonists was thereby confirmed.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1

ST adenosine A1 receptor locomotor behavior; blood **brain** barrier permeability A1 antagonist

IT Blood-**brain** barrier
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

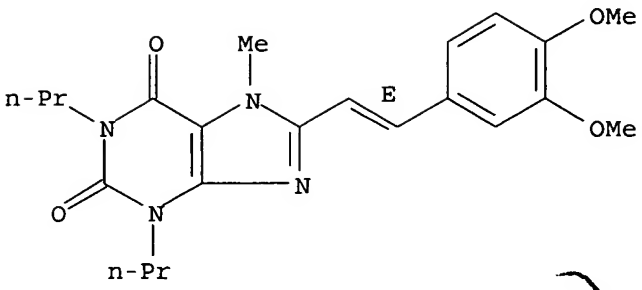
IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 146-77-0, 2-Chloroadenosine 961-45-5, 8-PT 35873-49-5, CPT 35920-39-9, 5'-N-Ethylcarboxamidoadenosine 36396-99-3 38594-96-6 41552-82-3, N6-Cyclopentyladenosine 75922-48-4, DPX 80206-91-3 89073-57-4 102146-07-6, DPCPX 121524-18-3, FK453 126828-50-0, APEC 136199-02-5, KW3902 137766-81-5, MDL102234 **141807-96-7**, KF17837 143881-08-7, FK352
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

IT **141807-96-7**, KF17837
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

RN 141807-96-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:224850 HCAPLUS
DOCUMENT NUMBER: 128:267779
TITLE: Evaluation of carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand
AUTHOR(S): Noguchi, Junko; Ishiwata, Kiichi; Wakabayashi, Shin-Ichi; Nariai, Tadashi; Shumiya, Seigo; Ishii, Shin-Ichi; Toyama, Hinako; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center and Department of Laboratory Animal Science, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173, Japan
SOURCE: Journal of Nuclear Medicine (1998), 39(3), 498-503
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 11C-labeled KF17837 ([7-methyl-11C](E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine) was evaluated as a PET ligand for mapping adenosine A2a receptors in the central nervous system (CNS). The regional **brain** distribution of [11C]KF17837 and the effect of adenosine antagonists on the distribution were measured in mice by the tissue sampling method. In rats, the regional **brain** uptake of [11C]KF17837 and the effect of carrier KF17837 was visualized by autoradiog. Imaging of the monkey **brain** with [11C]KF17837 was performed by PET. In mice, a high uptake of [11C]KF17837 was found in the striatum in which A2a receptors were highly enriched. The uptake was decreased by co-injection of carrier KF17837 or a xanthine-type A2a antagonist CSC but not by nonxanthine-type A2a antagonists ZM 241385 or SCH 58261, or an A1 antagonist KF15372. In the rat **brain**, [11C]KF17837 was accumulated higher in the striatum than in other **brain** regions, and the uptake was blocked by co-injection of carrier KF17837. In a monkey PET study, a high striatal uptake of radioactivity was observed Carbon-11-KF17837 binds to adenosine A2a receptors in the striatum. However, the presence of an unknown but specific binding site for xanthine-type compds. also was suggested in the other **brain** regions. The results also suggested that the in vivo receptor-binding sites of xanthine-type ligands are slightly different from those of nonxanthine-type A2a antagonists.

CC 8-9 (Radiation Biochemistry)
ST carbon 11 KF17837 adenosine receptor **brain**; PET imaging **brain** carbon 11 KF17837
IT **Brain**
Positron-emission tomography

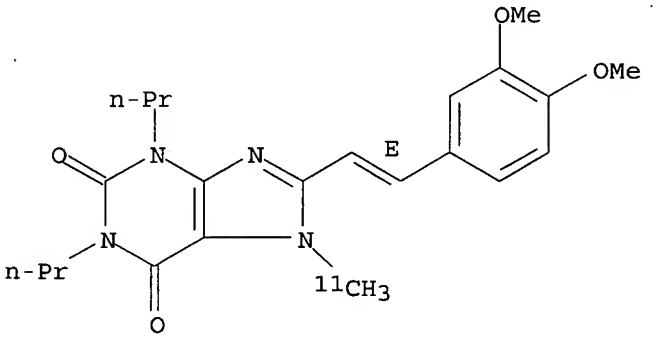
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:159025 HCAPLUS
DOCUMENT NUMBER: 130:322413
TITLE: Selective adenosine antagonists for mapping central nervous system adenosine receptors with positron emission tomography: carbon-11 labeled KF15372 (A1) and KF17837 (A2A)
AUTHOR(S): Suzuki, Fumio; Ishiwata, Kiichi
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, Japan
SOURCE: Drug Development Research (1998), 45(3/4), 312-323
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During the past decade, many neuroreceptors in humans and other animals have been visualized in vivo by positron emission tomog. (PET) with corresponding radioligands. Because adenosine is a neuromodulator, PET assessment of the adenosine receptor system offers us an opportunity to understand the neurotransmission system in general. The 11C-labeled selective adenosine A1 antagonists KF15372 and a 11C-Me derivative [11C]KF26345, and selective adenosine A2A antagonist KF17837 and KF18446

were evaluated in vivo as potential PET ligands for mapping CNS adenosine A1 and A2A receptors. [11C]KF15372 and [11C]KF263345: Tissue sampling and ex vivo autoradiog. (ARG) suggest that the regional **brain** distribution of [11C]KF15372 and [11C]KF26345 is consistent with that of the adenosine A1 receptors found in mice and rats. The **brain** uptake was competitively reduced by the coadministration of A1, but not by A2A antagonists. The ex vivo ARG on the rat model with unilateral orbital enucleation, visualized the A1 receptor deficiency in the presynaptic terminals. PET with these ligands visualized the A1 receptors in the monkey and cat **brain**. [11C]KF17837 and [11C]KF18446: In mice, a high uptake of two ligands was found in the striatum in which A2A receptors are highly enriched. The uptake was decreased by coinjection of carrier KF17837 or other xanthine-type A2A antagonists, but not by four nonxanthine-type A2A antagonists or A1 antagonists. In the rat **brain**, ex vivo ARG showed the A2A receptor-specific uptake of two ligands in the striatum. In PET studies of the monkey and cat **brain**, the A2A receptors in the striatum was clearly visualized. These pieces of evidence demonstrated the potential of 11C-labeled selective xanthine-type adenosine antagonists as PET ligands for mapping CNS adenosine A1 and A2A receptors.

CC 8-9 (Radiation Biochemistry)

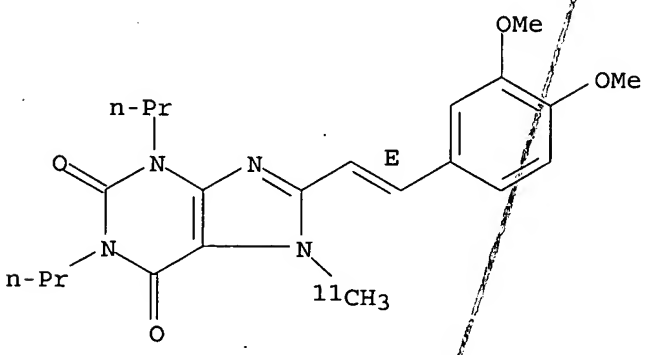
IT **Brain**
Positron-emission tomography
Purinoceptor antagonists
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

IT 170660-22-7 **179678-39-8** 188486-06-8 **223745-98-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

IT **179678-39-8 223745-98-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

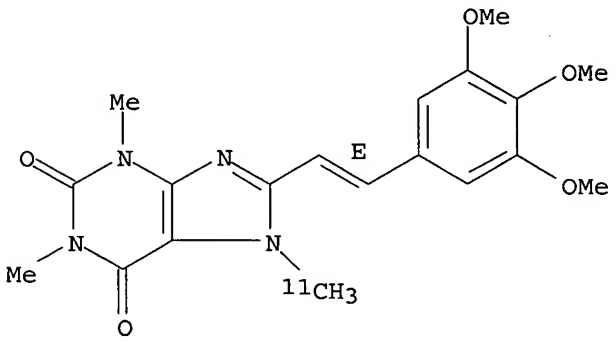
Double bond geometry as shown.



RN 223745-98-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:3847 HCAPLUS
DOCUMENT NUMBER: 128:85873
TITLE: In vivo evaluation of [11C]KF17837, a selective adenosine A2a antagonist, for mapping of CNS adenosine A2a receptor
AUTHOR(S): Noguchi, J.; Ishiwata, K.; Ishii, S.; Koike, N.; Wakabayashi, S.; Nariai, T.; Endo, K.; Suzuki, F.; Senda, M.
CORPORATE SOURCE: Positron Med. Cent., Tokyo Metropolitan Inst. Gerontol., Tokyo, 173, Japan
SOURCE: International Congress Series (1997), 1140(Role of Adenosine in the Nervous System), 201-206
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The carbon-11-labeled KF17837 ([7-methyl-11C](E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine) was evaluated as a radioligand for mapping adenosine A2a receptors in the central nervous system (CNS) by positron emission tomog. (PET). In mice, a high uptake of [11C]KF17837 was found in the striatum in which A2a receptors are highly enriched. The uptake was decreased by co-injection of carrier KF17837 or a xanthine type A2a antagonist CSC, but not by non-xanthine type A2a antagonists ZM 241385 or an A1 antagonist KF15372. In the rat **brain**, [11C]KF17837 accumulated higher in the striatum than in other **brain** regions and the uptake was blocked by co-injection of carrier KF17837. In a monkey PET study, a high striatal uptake of radioactivity was observed These pieces of evidence have demonstrated the potential of [11C]KF17837 as a PET ligand for mapping adenosine A2a receptors in the CNS.

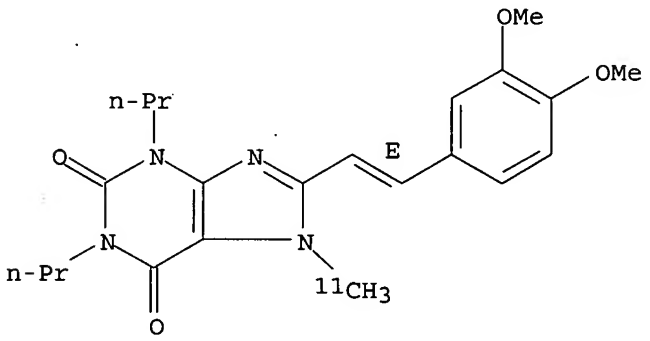
CC 8-9 (Radiation Biochemistry)
IT **Brain**
Positron-emission tomography
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)
IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified);

THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified);
THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

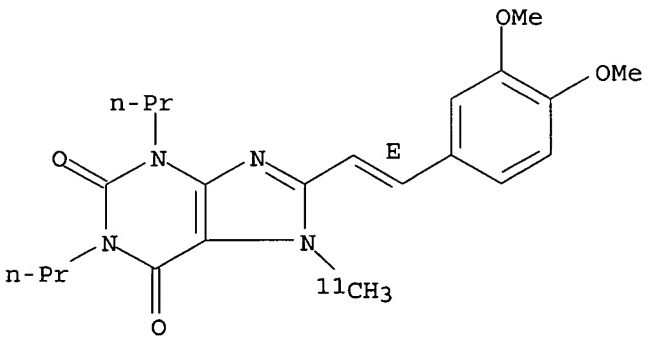
L34 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:237596 HCAPLUS
DOCUMENT NUMBER: 126:261014
TITLE: In vivo biodistribution of [N-11C-methyl]KF 17837 using 3-D-PET: evaluation as a ligand for the study of adenosine A2A receptors
AUTHOR(S): Stone-Elander, Sharon; Thorell, Jan-Olov; Eriksson, Lars; Fredholm, Bertil B.; Ingvar, Martin
CORPORATE SOURCE: KAROLINSKA PHARMACY, STOCKHOLM, S-17176, Swed.
SOURCE: Nuclear Medicine and Biology (1997), 24(2), 187-191
CODEN: NMBIEO; ISSN: 0883-2897
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KF 17837, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine, was 11C-labeled by methylation at N-7 of the nor-compound, KF 17440, using [11C]methyl iodide. Radiochem. conversions of 50% or 70-80% were obtained using sodium hydride or potassium carbonate, resp., as base. Total synthesis time was 40-45 min, including isolation by semipreparative liquid chromatog. Cerebral uptake of [N-11C-methyl]KF 17837 in Cynomolgus monkeys, evaluated using positron emission tomog. (PET), was so low that regional differences in distribution kinetics were revealed first after increasing injected dose 3-fold and using 3-D mode of data acquisition. At all times, the relative regional retention (maximum striatum:cerebellum: cortex ≈ 1.1:1:0.8 at 20 min) was considerably different from the known relative d. of A2A receptors in these regions. Radioactivity

decreased more rapidly in the cortex than in the striatum and cerebellum (by 20% vs. 3-7%, resp., between 5 and 50 min). Addition of carrier to [N-11C-methyl]KF 17837 only marginally affected the cerebral radiotracer uptake. By contrast, in the heart the initial tracer uptake was high and the elimination kinetics was enhanced by adding unlabeled carrier. We have thus shown that KF 17837 passes the blood-**brain** barrier, though to a very low extent. This fact and the apparently high nonspecific binding in vivo of [N-11C-methyl]KF 17837 in regions with low receptor densities limits its usefulness as a ligand for quantification of the adenosine A2A receptors in the primate **brain**.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine receptor PET; carbon 11 KF 17837 PET
IT **Brain**
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of **brain** adenosine A2A receptors)
IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of adenosine A2A receptors)
IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of adenosine A2A receptors)
RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 33 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97364156 EMBASE
DOCUMENT NUMBER: 1997364156
TITLE: Adenosine A(2A) receptors and neuroprotection.
AUTHOR: Ongini E.; Adami M.; Ferri C.; Bertorelli R.
CORPORATE SOURCE: E. Ongini, Schering-Plough Research Institute, San Raffaele Science Park, Via Olgettina 58, I-20132 Milan, Italy
SOURCE: Annals of the New York Academy of Sciences, (1997) Vol. 825, pp. 30-48.
Refs: 86

ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 971218
Last Updated on STN: 971218

AB The adenosine A(2A) receptor subtype is one of the four adenosine receptors that have been identified in the mammalian organism. In addition to being found in blood vessels, platelets and polymorphonuclear leukocytes, the A(2A) receptors are abundant in the central nervous system, especially in the striatum. The recent development of selective A(2A) receptor ligands, in particular of receptor antagonists, makes it possible to elucidate the function of A(2A) receptors in normal and altered conditions. Pharmacological studies have shown that A(2A) receptor antagonists are potentially effective for treatment of neurodegenerative processes such as Parkinson's disease. Their activity is attributed to the close anatomical and functional links between A(2A) receptors and dopaminergic pathways in the basal ganglia. More recently, A(2A) receptor antagonists have proved to be active in models of cerebral ischemia. While the mechanisms underlying the role of A(2A) receptors in the hypoxia/ischemia processes remains to be clarified, it is recognized that A(2A) receptor antagonists counteract the effects of excitatory aminoacids, which are massively released after cerebral ischemia. Another function of A(2A) receptors is related to protection from seizures, but further studies are needed to elucidate their specific interaction, if any, with neuronal excitability. Altogether, the great advance recently made with the discovery of selective A(2A) receptor ligands provides increasing information on the function of A(2A) receptors and opens new perspectives for treatment of neurological disorders.

CT Medical Descriptors:
*neuroprotection
brain ischemia: ET, etiology
complex partial seizure: ET, etiology
conference paper
drug selectivity
drug structure
human
nonhuman
parkinson disease: ET, etiology
structure activity relation
Drug Descriptors:
*adenosine a2a receptor: EC, endogenous compound
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): DV, drug development
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): PD, pharmacology
4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline: DV, drug development
4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline: PD, pharmacology
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: DV, drug development
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: PD, pharmacology

8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: DV, drug development
9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline: DV, drug development
9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline: PD, pharmacology
adenosine 5' (n ethylcarboxamide): DV, drug development
adenosine 5' (n ethylcarboxamide): PD, pharmacology
adenosine a2a receptor agonist: DV, drug development
caffeine: PD, pharmacology
dizocilpine

RN (2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide)) 120225-54-9; (4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline) 91896-57-0; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine) **141807-96-7**; (9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline) 104615-18-1; (adenosine 5' (n ethylcarboxamide)) 35920-39-9; (caffeine) 30388-07-9, 58-08-2; (dizocilpine) 77086-21-6

CN Cgs 21680; Kf 17837; Sch 58261; Cp 66713; Cgs 15943; Mk 801

L34 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:701996 HCAPLUS
DOCUMENT NUMBER: 126:1192
TITLE: Methods for protecting tissues and organs from ischemic damage
INVENTOR(S): Downey, James M.; Mullane, Kevin M.
PATENT ASSIGNEE(S): Gensia, Inc., USA; South Alabama Medical Science Foundation
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. 5, 443, 836. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5573772	A	19961112	US 1994-214942	19940317
US 5443836	A	19950822	US 1993-33310	19930315
PRIORITY APPLN. INFO.:			US 1993-33310 A2	19930315

AB Methods for protecting tissues and organs including the heart central nervous system, and kidney from ischemic damage are described and claimed based upon the recognition that protection against infarction is mediated by A3 rather than A1 adenosine receptors, as was previously thought, and that the receptor mediating protection in other organs and tissues has not been defined. Methods for selectively stimulating A3 adenosine receptors are described and claimed, as such selection is shown to prevent or substantially reduce cell death resulting from ischemia with or without reperfusion in humans. According to this invention, the A3 adenosine receptor is selectively stimulated by administering a compound which is an A3 adenosine receptor-selective agonist. Prevention of tissue death is also achieved by administering a compound which is a non-selective adenosine receptor agonist together with compds. that act as antagonists to the A1 and A2 adenosine receptor.

IC ICM A61F002-02
ICS A61K009-48; A61K009-20; A61K009-14
INCL 424423000
CC 1-8 (Pharmacology)

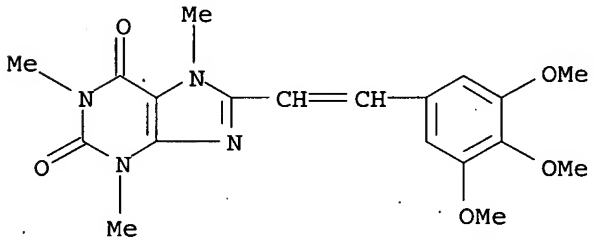
Section cross-reference(s): 63

IT **Brain, disease**
Heart, disease
Kidney, disease
(**ischemia**, preconditioning; methods for protecting tissues and organs from ischemic damage)

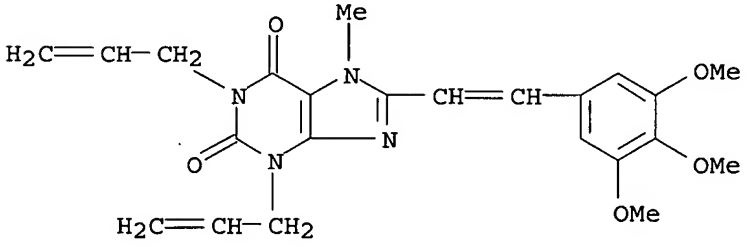
IT **31377-36-3** 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine 38594-97-7 41552-82-3, N6-Cyclopentyladenosine 96865-92-8, XAC 97905-57-2 98866-49-0 102146-07-6, Dpcpx 105834-00-2 116370-30-0, BW-A844U 120225-54-9, CGS 21680 124498-52-8, CGS 22492 124498-87-9, CGS 22989 131080-42-7, KF 15372 131933-18-1 133058-72-7, KFM 19 141696-90-4, N-0861 **158962-89-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for protecting tissues and organs from ischemic damage)

IT **31377-36-3 158962-89-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for protecting tissues and organs from ischemic damage)

RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



L34 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:368146 HCAPLUS
DOCUMENT NUMBER: 125:142663
TITLE: Synthesis and preliminary evaluation of [11C]KF17837,

a selective adenosine A2A antagonist

AUTHOR(S): Ishiwata, Kiichi; Noguchi, Junko; Toyama, Hinako; Sakiyama, Yojiro; Koike, Nobuaki; Ishii, Shin-Ichi; Oda, Keiichi; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio

CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Inst. Gerontology, Tokyo, 173, Japan

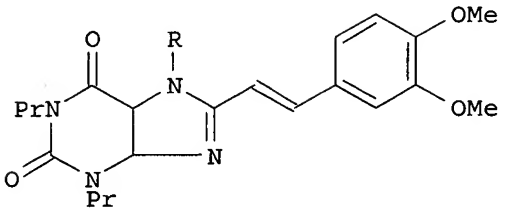
SOURCE: Applied Radiation and Isotopes (1996), 47(5/6), 507-511
CODEN: ARISEF; ISSN: 0969-8043

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB An 11C-labeled selective adenosine A2A antagonist, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-[11C]methylxanthine (I; R = 11CH3; [11C]KF17837), was prepared by reactions of (E)-8-(3,4-dimethoxystyryl)-1,3-dipropylxanthine (I; R = H)and [11C]methyl iodide with decay-corrected radiochem. yield of 19-50%, radiochem. purity of >99%, sp. act. of 17-100 GBq/μ mol and preparation time of 20-25 min. In mice, the myocardium showed the highest (13.4% ID/g) at at 5 min after i.v. injection, which decreased gradually with time. The specific myocardial uptake was visualized by γ-camera. In the **brain** region the radioactivity level was higher in the A2A receptors-rich striatum than in the cortex and cerebellum. The specific striatal uptake in rats was clearly demonstrated by PET. These results shown that [11C]KF17837 is a potential PET radioligand for mapping the adenosine A2A receptors in the heart and **brain**.

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST KF17837 radiolabeled prepn adenosine receptor antagonist; dimethoxystyrylmethylxanthine radiolabeled prepn adenosine receptor antagonist; dimethoxystyryldipropylxanthine alkylation radiolabeled methyl iodide; heart bioavailability radiolabeled KF17837; **brain** bioavailability radiolabeled KF17837; myocardium bioavailability radiolabeled KF17837; cortex bioavailability radiolabeled KF17837; cerebellum bioavailability radiolabeled KF17837; striatal uptake radiolabeled KF17837; PET radioligand KF17837 prepn

IT Animal tissue
Brain
Heart
(synthesis and biodistribution of [11C]KF17837 in)

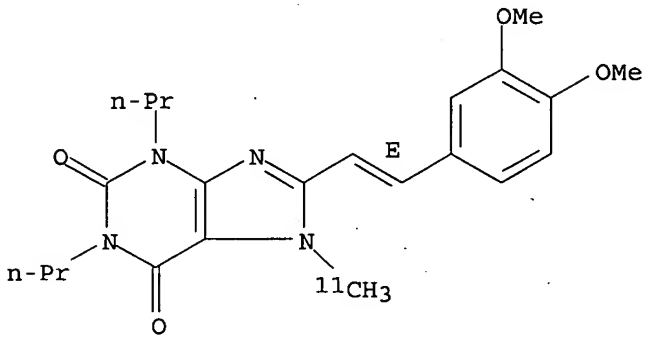
IT **179678-39-8P**, [7-11C]-(E)-8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and preliminary evaluation of [11C]KF17837 as a adenosine A2A antagonist)

IT **179678-39-8P**, [7-11C]-(E)-8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and preliminary evaluation of [11C]KF17837 as a adenosine A2A antagonist)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

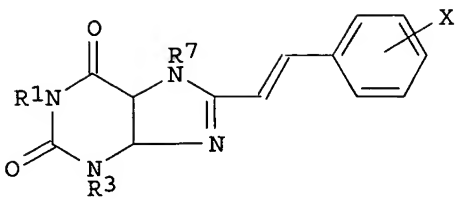


L34 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:446631 HCAPLUS
DOCUMENT NUMBER: 122:213859
TITLE: Preparation of 8-styryl-1,3,7-trialkylxanthine derivatives as A2-selective adenosine receptor antagonists
INVENTOR(S): Jacobson, Kenneth A.; Karton, Yishai; Gallo-Rodriguez, Carola; Fischer, Bilha; Van Galen, Philip J. M.; Maillard, Michel
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9425462	A1	19941110	WO 1994-US4876		19940503
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9467811	A1	19941121	AU 1994-67811		19940503
US 5861405	A	19990119	US 1994-335108		19941107
PRIORITY APPLN. INFO.:			US 1993-57086	A	19930503
			WO 1994-US4876	W	19940503

OTHER SOURCE(S): MARPAT 122:213859

GI



I

AB Title compds. (I; R1, R3, R7 = Me; X = 1-3 of amino, acylamino, diacylamino, halo, alkoxy, aminoalkoxy, aminoalkenyloxy, isothiocyanato, diazonium), and related compds., were prepared Thus, 1,3,7-trimethyl-8-(2-methoxystyryl)xanthine, prepared from 2-methoxycinnamic acid, showed Ki = 4760 nM and 267 nM for binding rat **brain** A1 and A2a receptors, resp.

IC ICM C07D473-08
ICS C07D473-12; C07D473-06; A61K031-52

CC 26-9 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 147700-11-6P 147700-24-1P **147700-25-2P 147700-30-9P 147700-31-0P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(adenosine receptor antagonist activity)

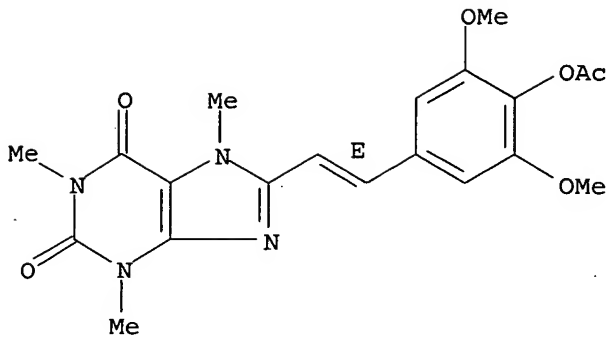
IT **51389-37-8P** 99765-13-6P 141807-86-5P **141807-96-7P**
147699-95-4P 147699-98-7P 147700-00-3P 147700-02-5P 147700-04-7P
147700-05-8P 147700-06-9P 147700-07-0P 147700-08-1P 147700-10-5P
147700-13-8P 147700-15-0P 147700-17-2P **147700-19-4P**
147700-21-8P 147700-23-0P **147700-26-3P 147700-27-4P**
147700-28-5P 147700-29-6P 147700-33-2P
147700-35-4P 147700-36-5P 147700-37-6P
147700-38-7P 147700-40-1P 147700-41-2P 147700-42-3P
147700-44-5P 147700-46-7P 147700-50-3P **147700-52-5P**
147700-54-7P 147700-55-8P 151539-31-0P 161826-76-2P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-styryl-1,3,7-trialkylxanthine derivs. as A2-selective adenosine receptor antagonists)

IT **147700-25-2P 147700-30-9P 147700-31-0P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(adenosine receptor antagonist activity)

RN 147700-25-2 HCAPLUS

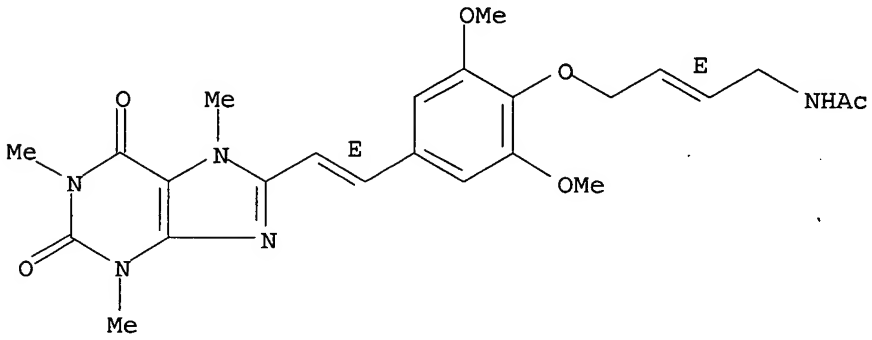
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



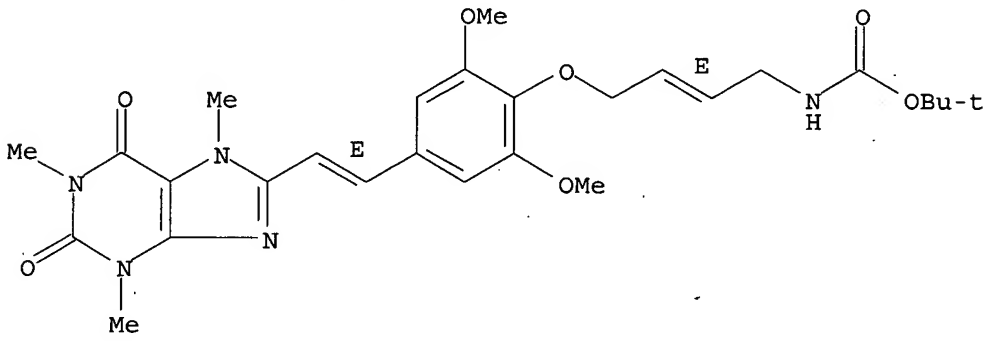
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

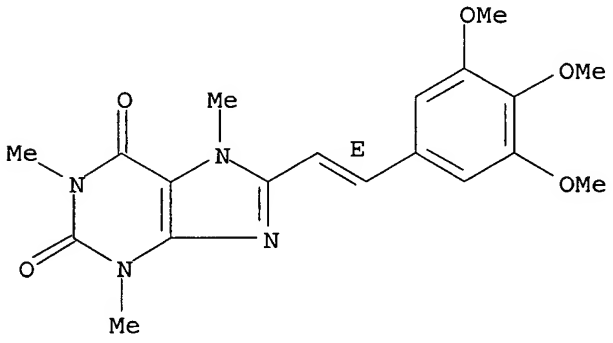


IT **51389-37-8P 141807-96-7P 147700-19-4P**
147700-26-3P 147700-27-4P 147700-28-5P
147700-29-6P 147700-33-2P 147700-35-4P

147700-36-5P 147700-37-6P 147700-38-7P
147700-40-1P 147700-52-5P 147700-54-7P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-styryl-1,3,7-trialkylxanthine derivs. as A2-selective adenosine receptor antagonists)

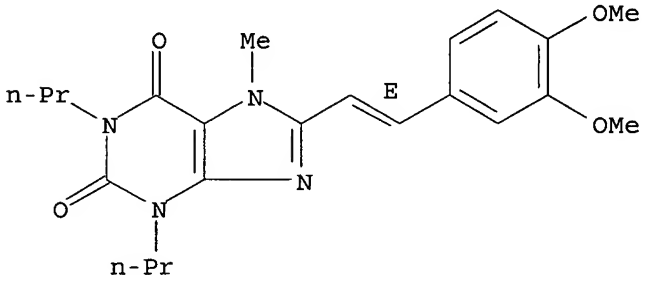
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



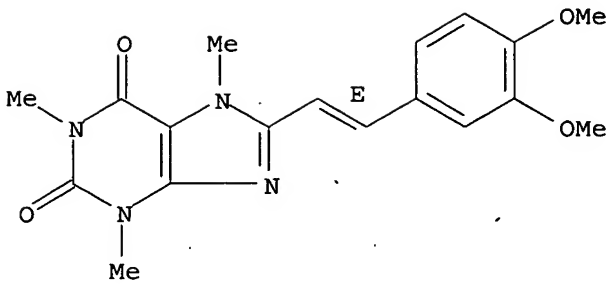
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



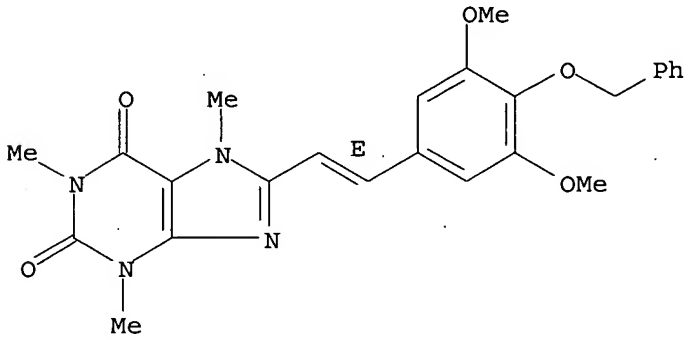
RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



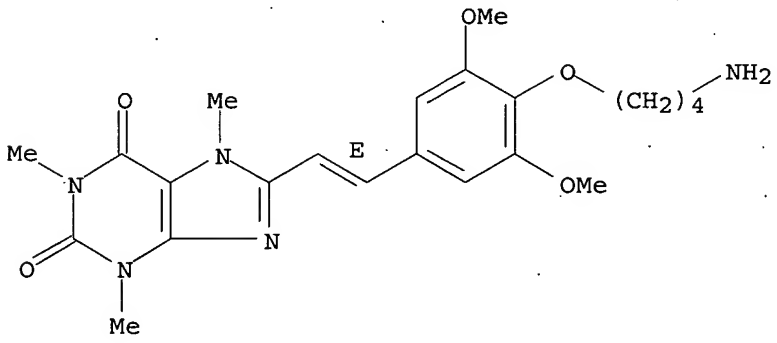
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



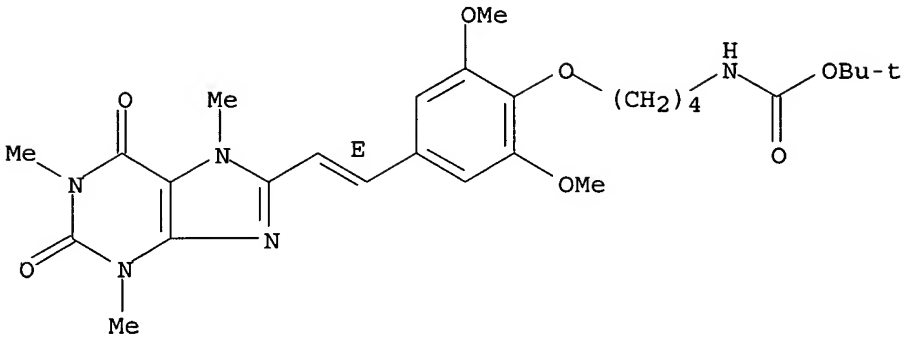
RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



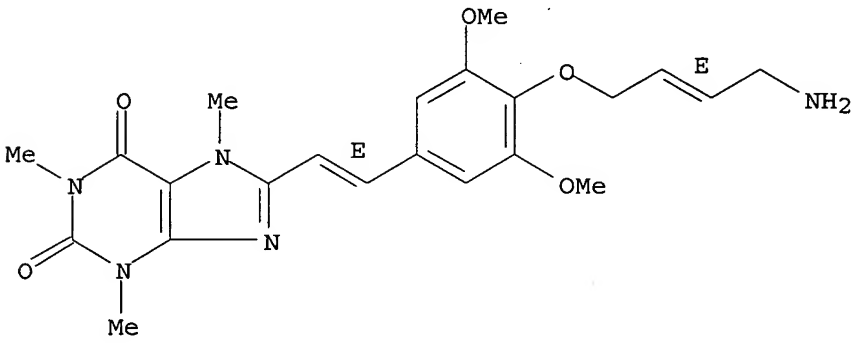
RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



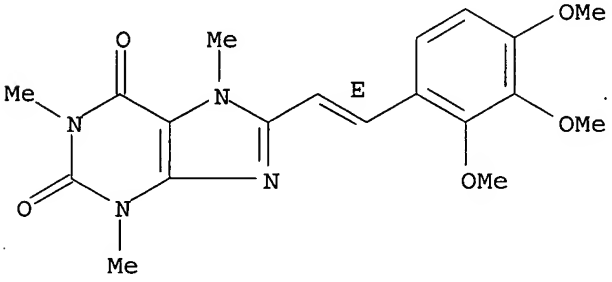
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



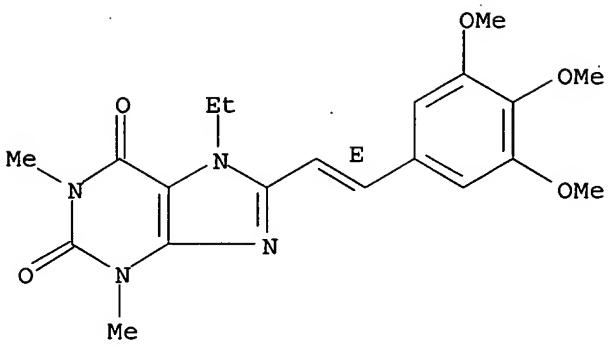
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



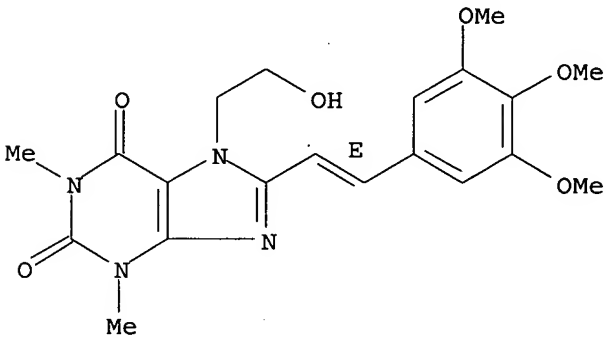
RN 147700-35-4 HCAPLUS
CN 1H-Purine-2,6-dione, 7-ethyl-3,7-dihydro-1,3-dimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



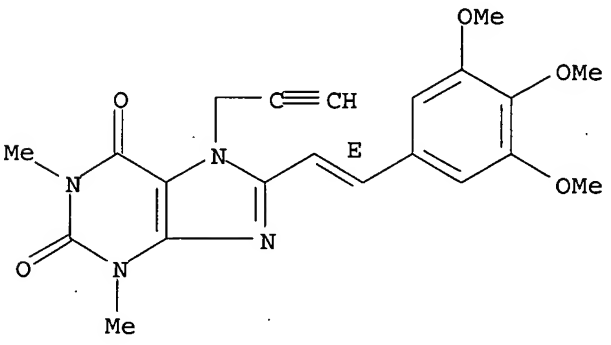
RN 147700-36-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-(2-hydroxyethyl)-1,3-dimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



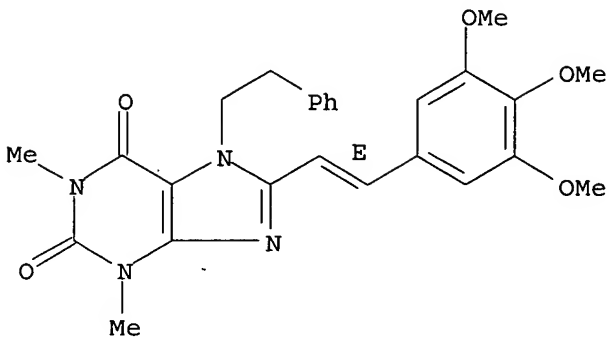
RN 147700-37-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(2-propynyl)-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



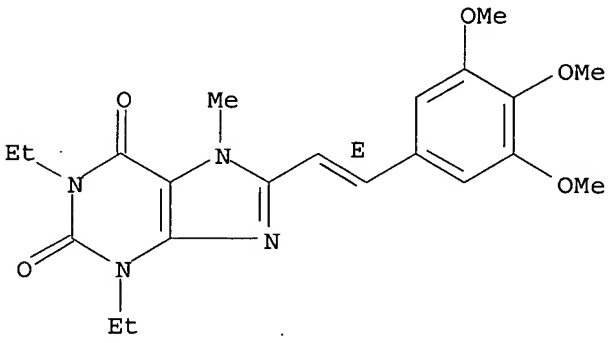
RN 147700-38-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(2-phenylethyl)-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



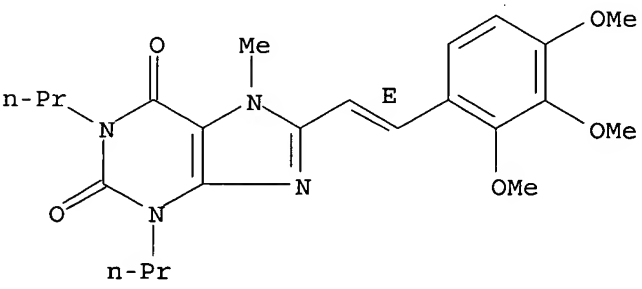
RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



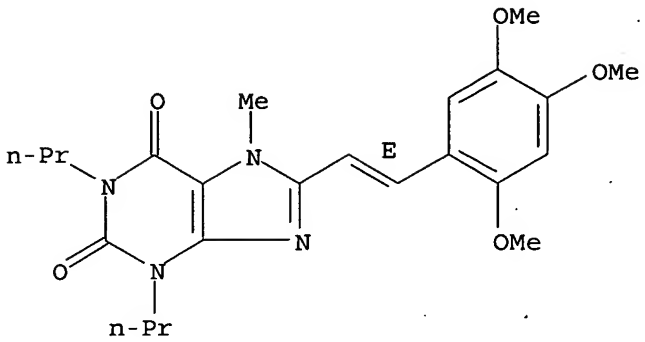
RN 147700-52-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-dipropyl-8-[2-(2,3,4-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-54-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-dipropyl-8-[2-(2,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



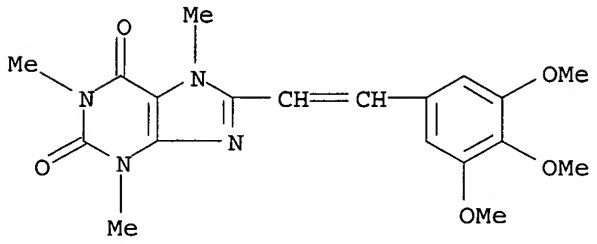
L34 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:672194 HCAPLUS
DOCUMENT NUMBER: 121:272194
TITLE: Methods for protecting tissues and organs from ischemic damage
INVENTOR(S): Downey, James M.; Mullane, Kevin M.
PATENT ASSIGNEE(S): Gensia, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421195	A1	19940929	WO 1994-US2854	19940315
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5443836	A	19950822	US 1993-33310	19930315
AU 9463662	A1	19941011	AU 1994-63662	19940315
EP 689405	A1	19960103	EP 1994-910956	19940315
R: CH, DE, FR, GB, IT, LI, NL				

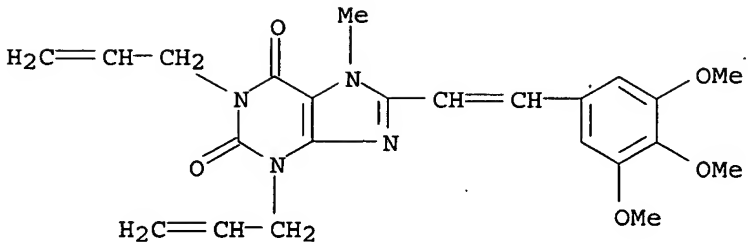
PRIORITY APPLN. INFO.: US 1993-33310 A 19930315
WO 1994-US2854 W 19940315

AB Methods for protecting tissues and organs including the heart, central nervous system, and kidney from ischemic damage are described and claimed based upon the recognition that protection against infarction is mediated by A3 rather than A1 adenosine receptors, as was previously thought, and that the receptor mediating protection in other organs and tissues has not been defined. Methods for selectively stimulating A3 adenosine receptors are described and claimed, as such selection is shown to prevent or substantially reduce cell death resulting from ischemia with or without reperfusion in humans. According to this invention, the A3 adenosine receptor is selectively stimulated by administering a compound which is an A3 adenosine receptor-selective agonist. Prevention of tissue death is also achieved by administering a compound which is a non-selective adenosine receptor agonist together with compds. that act as antagonists to the A1 and A2 adenosine receptor.

IC ICM A61F002-02
ICS A61K009-14; A61K009-20; A61K009-48; A61M031-00
CC 1-12 (Pharmacology)
ST A3 adenosine receptor agonist; A1 adenosine receptor antagonist; A2 adenosine receptor antagonist; ischemic damage organ; **brain** heart kidney ischemic damage
IT **Ischemia**
(organ; A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT **Brain, disease**
Heart, disease
Kidney, disease
(**ischemia**, A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT 58-61-7, Adenosine, biological studies **31377-36-3** 35920-39-9, 5'-N-Ethylcarboxamidoadenosine 38594-96-6 102146-07-6, 1,3-Dipropyl-8-cyclopentylxanthine 105834-00-2 116370-30-0, BW-A 844U 131080-42-7, KF 15372 133058-72-7, KFM 19 141696-90-4, N-0861 152918-15-5 152918-16-6 152918-17-7 152918-18-8 158962-88-0 **158962-89-1**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT **31377-36-3 158962-89-1**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



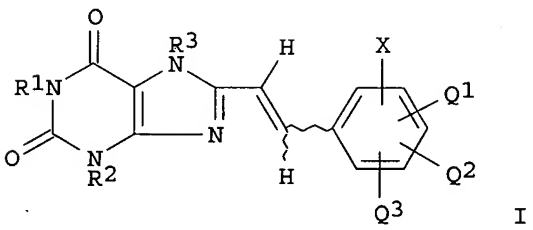
RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



L34 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:168999 HCAPLUS
DOCUMENT NUMBER: 122:81388
TITLE: (Styryl)xanthine-derivatives adenosine A2 receptor antagonists
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Koike, Nobuaki; Kase, Hiroshi; Nakamura, Joji; Shiozaki, Shizaki; Nonaka, Hiromi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Can. Pat. Appl., 69 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2112031	AA	19940625	CA 1993-2112031	19931221
JP 06239862	A2	19940830	JP 1993-316132	19931216
JP 3165769	B2	20010514		
NO 9304792	A	19940627	NO 1993-4792	19931223
EP 607607	A1	19940727	EP 1993-120842	19931223
EP 607607	B1	19960918		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 143019	E	19961015	AT 1993-120842	19931223
US 5670498	A	19970923	US 1995-527497	19950913

PRIORITY APPLN. INFO.: JP 1992-344116 A 19921224
US 1993-171602 B1 19931222
OTHER SOURCE(S): MARPAT 122:81388
GI



I

AB The title compds. [I; Q1-Q3 = H, lower alkyl, lower alkoxy, halogen; R1-R3 = H, lower alkyl; X = COR4, SO2R5; R4 = H, HO, lower alkyl, lower alkoxy; R5 = (un)substituted NH2, etc.], useful as adenosine A2 receptor

antagonists for the treatment of Parkinson's disease (no data), depression (no data), etc., are prepared and I-containing formulations presented. Thus, (E)-8-(3-acetylstyryl)-1,3-diethyl-7-methylxanthine, m.p. 221.4-221.8°, was prepared and demonstrated 85% inhibition. of 3H-CGS 21680 binding to rat **brain**-derived adenosine A2 receptors at 10-7 mol (Ki = 13 nM).

IC ICM C07D473-04
ICS A61K031-52

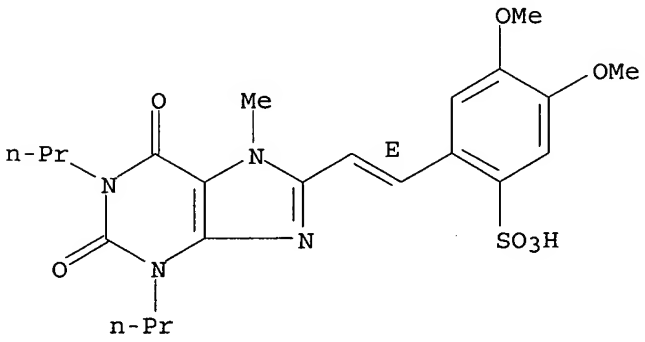
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **160434-09-3P 160434-10-6P 160434-11-7P**
160434-12-8P 160434-14-0P 160434-15-1P
160434-16-2P 160434-17-3P **160434-18-4P 160434-19-5P**
160434-20-8P 160434-21-9P 160434-23-1P
160434-24-2P 160434-25-3P 160434-26-4P 160434-27-5P
160434-28-6P 160434-29-7P 160434-30-0P 160434-31-1P 160434-32-2P
160434-33-3P 160434-34-4P 160434-35-5P 160434-36-6P 160434-37-7P
160434-38-8P 160434-39-9P 160434-40-2P 160471-61-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(styrylxanthine adenosine A2 receptor antagonists)

IT **160434-09-3P 160434-10-6P 160434-11-7P**
160434-12-8P 160434-14-0P 160434-15-1P
160434-18-4P 160434-19-5P 160434-20-8P
160434-21-9P 160434-23-1P 160434-24-2P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(styrylxanthine adenosine A2 receptor antagonists)

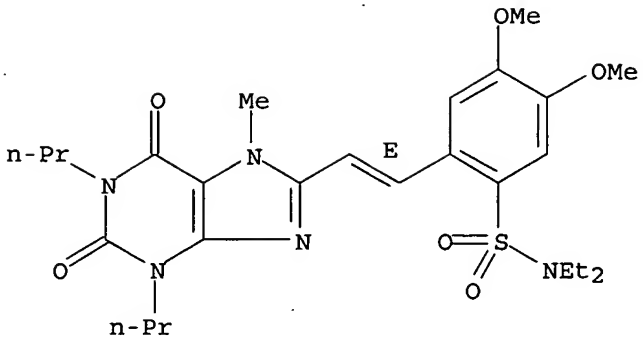
RN 160434-09-3 HCAPLUS
CN Benzenesulfonic acid, 4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



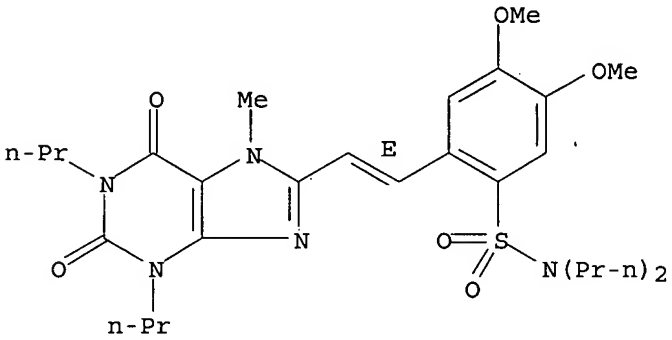
RN 160434-10-6 HCAPLUS
CN Benzenesulfonamide, N,N-diethyl-4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



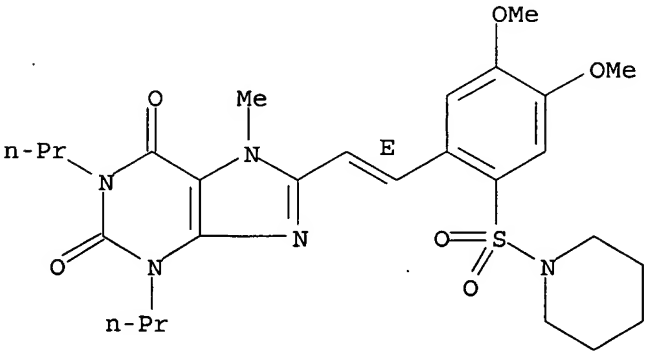
RN 160434-11-7 HCAPLUS
CN Benzenesulfonamide, 4,5-dimethoxy-N,N-dipropyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 160434-12-8 HCAPLUS
CN Piperidine, 1-[[4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]phenyl]sulfonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



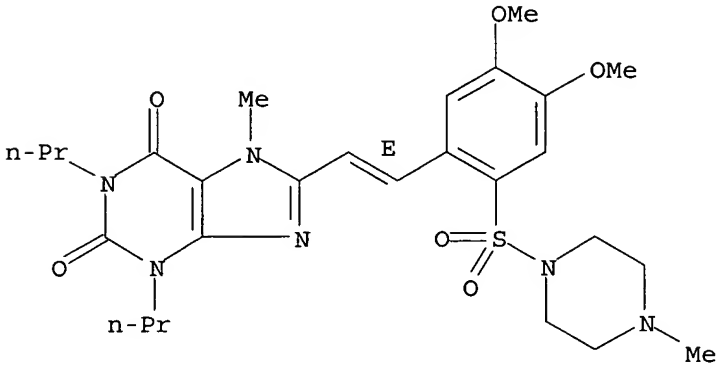
RN 160434-14-0 HCAPLUS
CN Piperazine, 1-[[4,5-dimethoxy-2-[(1E)-2-(2,3,6,7-tetrahydro-7-methyl-2,6-

dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]phenyl]sulfonyl]-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 160434-13-9
CMF C27 H38 N6 O6 S

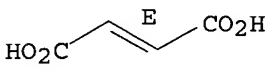
Double bond geometry as shown.



CM 2

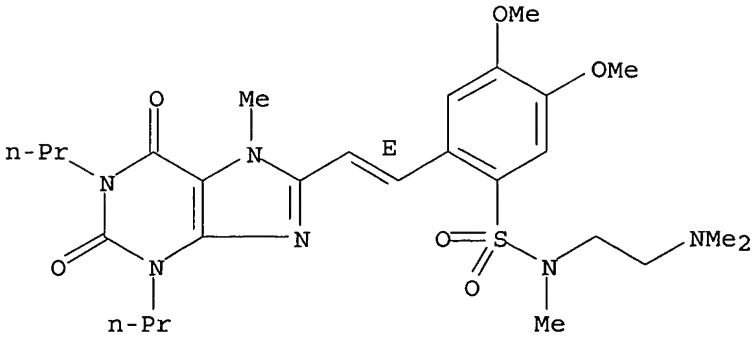
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 160434-15-1 HCAPLUS
CN Benzenesulfonamide, N-[2-(dimethylamino)ethyl]-4,5-dimethoxy-N-methyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

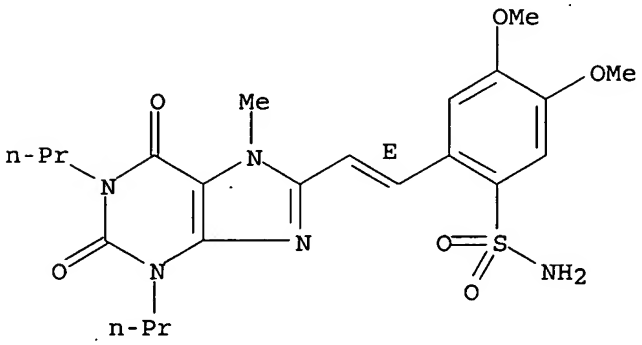
Double bond geometry as shown.



RN 160434-18-4 HCAPLUS

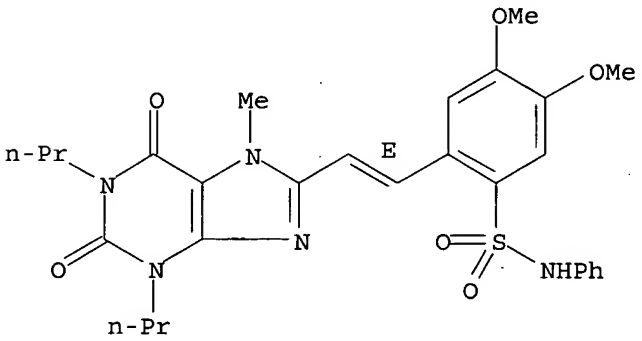
CN Benzenesulfonamide, 4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



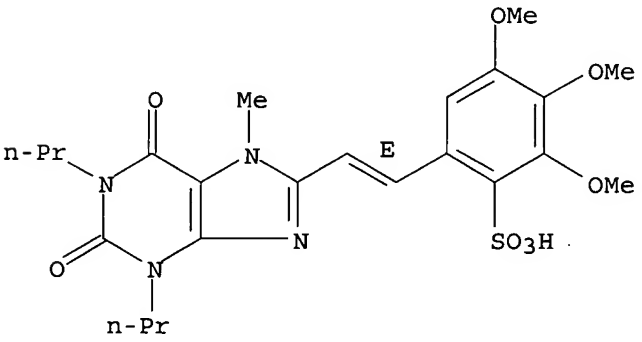
RN 160434-19-5 HCAPLUS
CN Benzenesulfonamide, 4,5-dimethoxy-N-phenyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



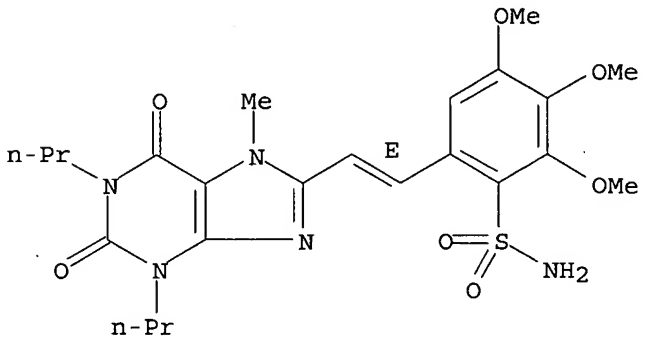
RN 160434-20-8 HCAPLUS
CN Benzenesulfonic acid, 2,3,4-trimethoxy-6-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 160434-21-9 HCAPLUS
CN Benzenesulfonamide, 2,3,4-trimethoxy-6-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 160434-23-1 HCAPLUS
CN Benzenesulfonamide, N-[2-(dimethylamino)ethyl]-2,3,4-trimethoxy-N-methyl-6-[(1E)-2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

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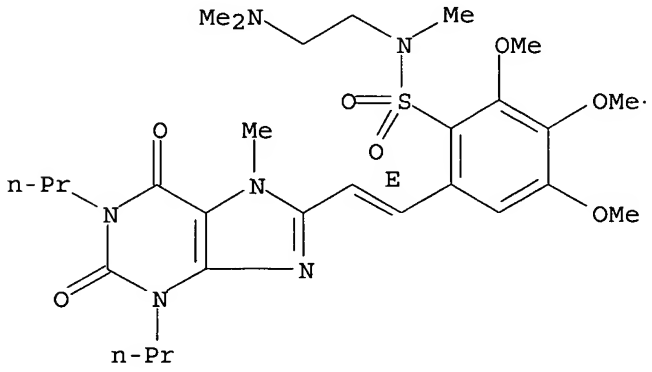
CRN 160434-22-0
CMF C28 H42 N6 O7 S

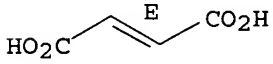
Double bond geometry as shown.



CM 2

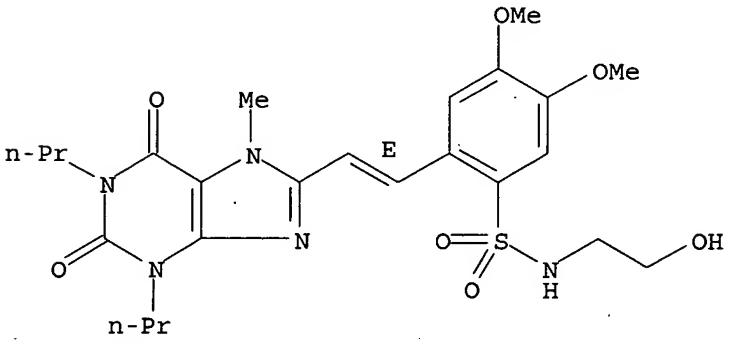
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 160434-24-2 HCAPLUS
CN Benzenesulfonamide, N-(2-hydroxyethyl)-4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:237592 HCAPLUS
DOCUMENT NUMBER: 122:23168
TITLE: Binding of [3H]KF17837S, a selective adenosine A2 receptor antagonist, to rat **brain** membranes
AUTHOR(S): Nonaka, Hiromi; Mori, Akihisa; Ichimura, Michio; Shindou, Tomomi; Yanagawa, Koji; Shimada, Junichi; Kase, Hiroshi
CORPORATE SOURCE: Pharmaceutical Res. Lab., Kyowa Hakko Kogyo Co., Ld., Shizuoka, 411, Japan
SOURCE: Molecular Pharmacology (1994), 46(5), 817-22
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential of 8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-[3H]methylxanthine ([3H]KF17837S) a a highly selective antagonist radioligand for the adenosine A2A receptor was examined and compared with the properties of the adenosine A2A receptor agonist radioligand 2-[p-(2-[3H]carboxyethyl)phenethylamino]-5'-N-ethylcarboxamidoadenosine ([3H]CGS21680). [3H]KF17837S specific binding to rat striatal membranes was saturable and reversible. Saturation studies showed that the binding of [3H]KF17837S occurred at a single site, with high affinity (Kd, 7.1 nM) and limited capacity (Bmax, 1.3 pmol/mg of protein). Adenosine receptor antagonist ligands competed with the binding of 1 nM [3H]KF17837S with the following order of activity: CGS15943 > KR17837S > N-[2-(dimethylamino)ethyl]-N-methyl-4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)benzenesulfonamide ≥ xanthine amine congener > 8-cyclopentyl-1,3-dipropylxanthine > 8-(noradamantan-3-yl)-1,3-dipropylxanthine > caffeine. Adenosine receptor agonists inhibited [3H] KF17837S binding in the following order: 5'-N-ethylcarboxamidoadenosine ≥ CGS21680 > 2-phenylaminoadenosine ≥ (R)-N6-phenylisopropyladenosine > N6-cyclopentyladenosine > (S)-N6-phenylisopropyladenosine. The Ki values of the antagonists for [3H]KF17837S binding and the rank order of potency were similar to those for [3H]CGS21680 binding. The affinities of the agonists were lower with [3H]KF17837S binding than with [3H] CGS21680 binding. However, a strong

pos. correlation (r = 0.98) was observed between the pharmacol. profiles for these two radioligand assays. The inhibition curve for CGS21680 was best fitted to a two-component binding model and addition of GTP shifted the inhibition curve to the right, suggesting that [3H]KF17837S labeled two agonist coupling states. Other pharmacol. agents had negligible affinities for the [3H]KF17837S binding site. Autoradiog. study of [3H]KF17837S binding using rat **brain** sections revealed that the binding site was highly enriched in the striatal region. The data indicate that [3H]KF 17837S labels the adenosine A2A receptor in rat **brain**.

CC 1-2 (Pharmacology)
Section cross-reference(s): 2, 8, 9

IT **Brain**
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

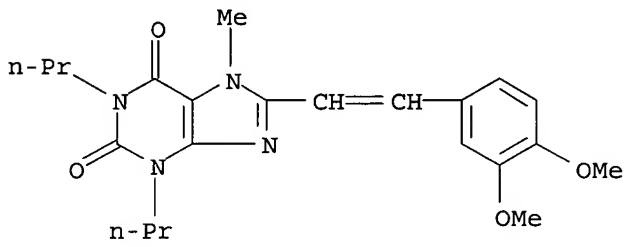
IT Neurotransmitter antagonists
(purinergic A2, characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

IT **149744-74-1**, KF 17837S
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

IT **149744-74-1**, KF 17837S
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

RN 149744-74-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)



L34 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1994:571191 HCAPLUS
DOCUMENT NUMBER:	121:171191
TITLE:	Inhibition by KF17837 of adenosine A2A receptor-mediated modulation of striatal GABA and ACh release
AUTHOR(S):	Kurokawa, Masako; Kirk, Ian P.; Kirkpatrick, Karen A.; Kase, Hiroshi; Richardson, Peter J.
CORPORATE SOURCE:	Dept. of Pharmacology, Univ. of Cambridge, Cambridge, CB2 1QJ, UK
SOURCE:	British Journal of Pharmacology (1994), 113(1), 43-8 CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The effect of the A2A adenosine receptor agonist, 2-p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamidoadenosine (CGS 21680) on the potassium-evoked release of [3H]-GABA from nerve terminals derived from the caudate-putamen and the globus pallidus of the rat was compared. In both prepns. CGS 21680 (1 nM) inhibited the [3H]-GABA release evoked by 15 mM KCl but had no effect on that evoked by 30 mM KCl. The ability of CGS 21680 (1 nM) to inhibit the release of [3H]-GABA from striatal nerve terminals was unaffected by the presence of the GABA receptor antagonists, bicuculline (10 μM), phaclofen (100 μM) and 2-hydroxysaclofen (100 μM). Similarly the opioid receptor antagonist, naloxone (10 μM), the adenosine A1 receptor antagonist, 8-cyclopentyl-1,3-dipropylxanthine (DPCPX, 40 nM), and the cholinoceptor antagonists, mecamylamine (10 μm) and atropine (100 nM), had no effect on this inhibition. The ability of CGS 21680 (0.1 nM) to stimulate the release of [3H]-acetylcholine ([3H]-ACh) from striatal nerve terminals was unaffected by the presence of bicuculline (10 μM), 2-hydroxysaclofen (100 μM), phaclofen (100 μM), naloxone (10 μM) and DPCPX (4 nM). The novel A2A receptor antagonist, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine (KF 17837), blocked the CGS 21680 (1 nM)-induced inhibition of [3H]-GABA efflux with an EC50 of approx. 30 nM and also antagonized the CGS 21680 (0.1 nM)-induced stimulation of [3H]-ACh release with an EC50 of approx. 0.3 nM. It is concluded that the A2A adenosine receptor is present on both GABAergic and cholinergic nerve terminals of the rat striatum and that in both the caudate-putamen and the globus pallidus this receptor inhibits [3H]-GABA release. No evidence was seen for a difference in the ligand binding sites of this receptor in the 2 groups of nerve terminals.

CC 2-8 (Mammalian Hormones)

IT **Brain**
(globus pallidus, adenosine A2A receptor modulation of potassium-evoked GABA release from)

IT **Brain**
(neostriatum, adenosine A2A receptor modulation of potassium-evoked GABA release from)

IT **Brain**
(striatum, adenosine A2A receptor modulation of acetylcholine and GABA release from)

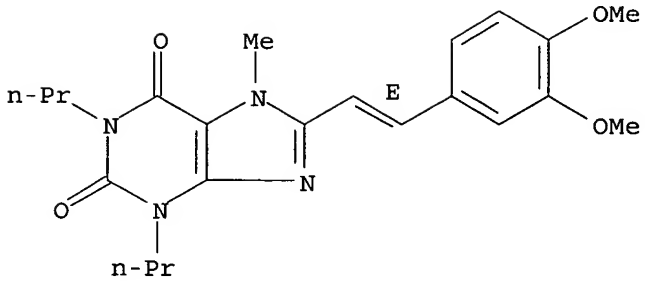
IT **141807-96-7**, KF 17837
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2A receptor-mediated modulation of acetylcholine and GABA release from striatum inhibition by)

IT **141807-96-7**, KF 17837
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2A receptor-mediated modulation of acetylcholine and GABA release from striatum inhibition by)

RN 141807-96-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.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*                                                                       *
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* available and contains the CA role and document type information.     *
*                                                                       *
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Experimental and calculated property data are now available. For more
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FILE LAST UPDATED: 4 Jul 2005  (20050704/ED)

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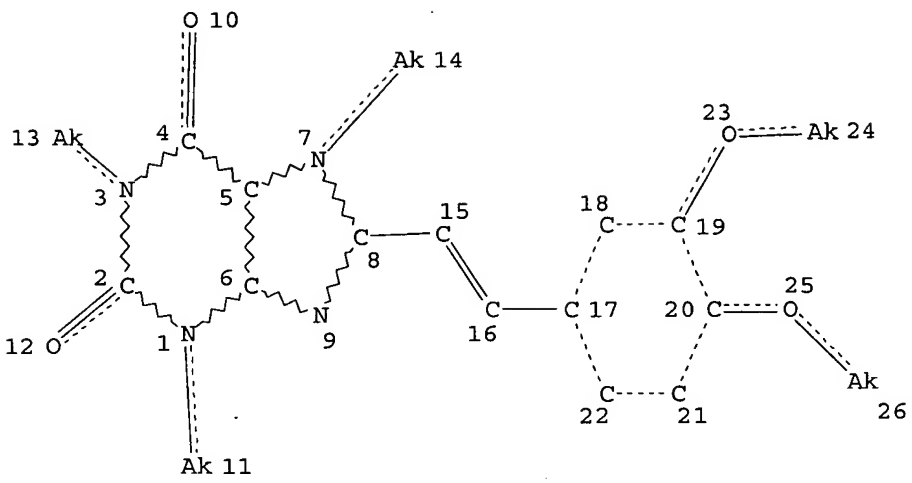
L7 STR



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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
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L19 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (L16 OR L17 OR BRAIN?)

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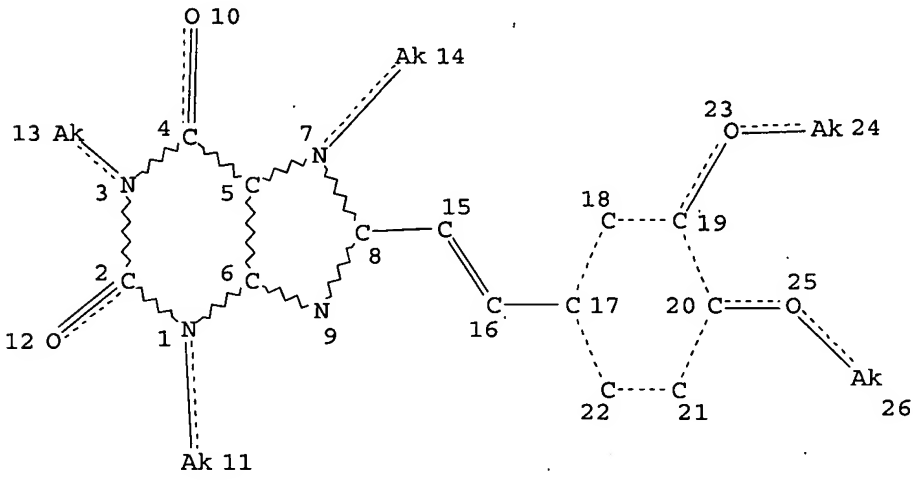
L7 STR



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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  26

STEREO ATTRIBUTES: NONE
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                 ?INFARC? OR ?HYPOX? OR ?NEURODEGEN?)
L29            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L26 AND L28


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FILE 'EMBASE' ENTERED AT 15:52:02 ON 05 JUL 2005

PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L29
L34 40 DUP REMOVE L19 L29 (0 DUPLICATES REMOVED)

=> d ibib abs hitind hitstr 1-40 L34

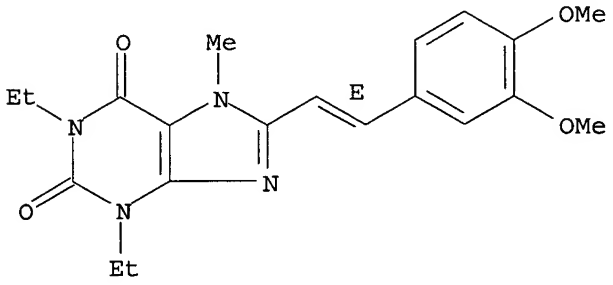
L34 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:646209 HCAPLUS
DOCUMENT NUMBER: 142:211382
TITLE: Novel Diamino Derivatives of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as Potent and Selective Adenosine A2a Receptor Antagonists
AUTHOR(S): Vu, Chi B.; Pan, Deborah; Peng, Bo; Kumaravel, Gnanasambandam; Smits, Glenn; Jin, Xiaowei; Phadke, Deepali; Engber, Thomas; Huang, Carol; Reilly, Jennifer; Tam, Stacy; Grant, Donna; Hetu, Gregg; Petter, Russell C.
CORPORATE SOURCE: Department of Medicinal Chemistry, Biogen Idec Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 2009-2018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Piperazine derivs. of 2-furanyl[1,2,4]triazolo[1,5-a][1,3,5]triazine have recently been demonstrated to be potent and selective adenosine A2a receptor antagonists with oral activity in rodent models of Parkinson's disease. We have replaced the piperazinyl group with a variety of linear, monocyclic, and bicyclic diamines. Of these diamines, (R)-2-(aminomethyl)pyrrolidine is a particularly potent and selective replacement for the piperazinyl group. With this diamine component, we have been able to prepare numerous analogs with low nanomolar affinity toward the A2a receptor and good selectivity with respect to the A1 receptor (>200-fold in some cases). Selected analogs from this series of [1,2,4]triazolo[1,5-a][1,3,5]triazine have now been shown to be orally active in the mouse catalepsy model.
CC 1-3 (Pharmacology)
Section cross-reference(s): 2, 14
IT **Brain**
(cerebral cortex; novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)
IT 139180-30-6, ZM-241385 **155270-99-8**, KW-6002 160098-96-4, SCH-58261 745072-66-6

RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)

IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(novel diamino derivs. of [1,2,4]Triazolo[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists)

RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:214290 HCAPLUS
DOCUMENT NUMBER: 142:404037
TITLE: KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse
AUTHOR(S): Pierri, Mette; Vaudano, Elisabetta; Sager, Thomas; Englund, Ulrica
CORPORATE SOURCE: H. Lundbeck A/S, Pharmacology Target Research, Valby, DK-2500, Den.
SOURCE: Neuropharmacology (2005), 48(4), 517-524
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The risk of Parkinson's disease (PD) is associated with a lower intake of caffeine, a non-selective adenosine A2A antagonist. In agreement, genetic or pharmacol. inactivation of adenosine A2A receptors in animal models of PD has demonstrated both symptomatic and neuroprotective effects. These findings and the lack of disease modifying therapies have led to intense research on adenosine A2A antagonists as a novel treatment for PD. In the present study the neuroprotective effect of the A2A receptor antagonist KW-6002 was investigated using different models of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in mice, which induced dopaminergic terminal and or dopaminergic cell loss and inflammation. Treatment with KW-6002 prevented the loss of dopaminergic striatal terminals and nigral cell bodies and inhibited the nigral microglia activation. Our results confirm previous findings that pharmacol. inactivation of A2A receptors inhibits MPTP-induced dopaminergic damage at the level of striatum. In addition, we demonstrate for the first time that, after MPTP treatment in

mice, an A2A antagonist is neuroprotective, and has anti-inflammatory effects, at the level of the substantia nigra. Thus, our data further support the use of A2A receptor antagonists as a novel neuroprotective therapy for PD.

CC 1-11 (Pharmacology)

IT Anti-inflammatory agents
Brain
(substantia nigra; KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

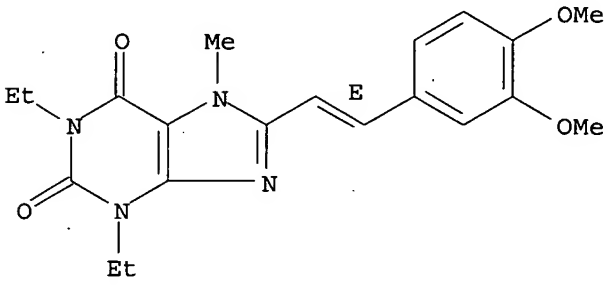
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(KW-6002 protects from MPTP induced dopaminergic toxicity in the mouse)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:570030 HCAPLUS
DOCUMENT NUMBER: 141:99661
TITLE: Identification of compounds suitable as agonists and/or antagonists of adenosine A2A receptor coupled to specific G proteins, and use of identified compounds in treatment of various disorders in mammals
INVENTOR(S): Fredholm, Bertil B.; Kull, Bjoern
PATENT ASSIGNEE(S): Actar Ab, Swed.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058974	A1	20040715	WO 2003-SE2086	20031229

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2002-436480P P 20021227

AB The invention discloses a method of drug screening to select chemical compds. suitable as receptor agonists or antagonists that act on a receptor belonging to the family of G protein coupled receptors. The method involves constructing a biol. preparation comprising a receptor coupled to a specific G protein, bringing a compound in contact with said preparation, and studying the functional properties of said compound in biol. preparation The invention also discloses the use of identified compound as a drug for treatment of CNS disorders, cardiovascular disorders, inflammatory disorders, metabolic disorders, cancer and other hyperproliferative disorders in a mammal. Specifically, the invention discloses a novel approach to identify and test compds. based on changes in adenosine A2A receptor binding dependent on the nature of the coupled G protein. The invention related that this approach seemed feasible due to the evidence that G proteins, such as Gs, Gi or Golf, influence the binding properties of A2A receptors. The invention also related that a truly efficient drug mol., in addition to affinity towards A2A, can be specific towards the different G proteins associated with A2A. In the examples, the invention used transformed CHO cells expressing A2A receptors linked to Gs or Golf G proteins, and demonstrated the existence of G-protein-dependent ligand specificity. Specifically, the examples demonstrated that substance KF 17837 has higher affinity to the A2A-Golf complex in striatum than to A2A-Gs complex in leukocytes. The examples also showed how some compds. influence A2A receptors coupled to Golf more readily than A2A receptors coupled to Gs.

IC ICM C12N015-12
ICS G01N033-53; C12Q001-68; C07K014-705; A61P025-16; A61P037-00
CC 1-1 (Pharmacology)
Section cross-reference(s): 2, 14
IT Lymphocyte
(binding of chemical compds. to adenosine A2A receptors in membrane preparation
derived from pig **brain** (A2A receptors coupled to Golf) or
from pig lymphocytes (A2A receptors coupled to Gs))
IT **Brain**
(corpus striatum; binding of chemical compds. to adenosine A2A receptors in membrane preparation derived from pig **brain** (A2A receptors coupled to Golf) or from pig lymphocytes (A2A receptors coupled to Gs))
IT 146-77-0 446-72-0 17318-31-9 18732-09-7 18732-18-8 20125-40-0
35788-27-3 46155-90-2 53296-10-9 91896-57-0 126235-09-4
141018-30-6 144930-92-7 380878-34-2 381701-48-0 400087-52-7
721401-37-2 721401-39-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of chemical compds. to adenosine A2A receptors in membrane preparation
derived from pig **brain** (A2A receptors coupled to Golf) or
from pig lymphocytes (A2A receptors coupled to Gs))
IT **141807-96-7**, KF 17837
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance KF 17837 has higher affinity to A2A receptor -Golf complex

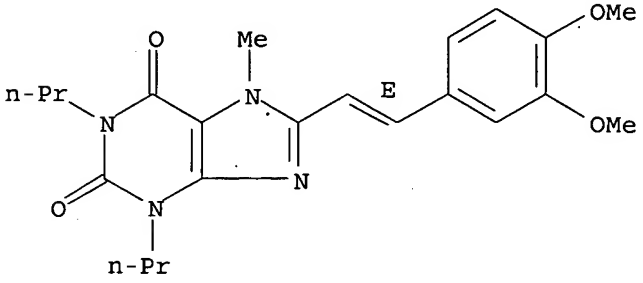
in striatum than to A2A-Gs complex in leukocytes)

IT **141807-96-7**, KF 17837
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance KF 17837 has higher affinity to A2A receptor -Golf complex in striatum than to A2A-Gs complex in leukocytes)

RN 141807-96-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:566535 HCAPLUS
DOCUMENT NUMBER: 141:99728
TITLE: A method using (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine for treating behavioral disorders
INVENTOR(S): Shiozaki, Shizuo; Shimada, Junichi; Kase, Hiroshi; Shindo, Mayumi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058139	A2	20040715	WO 2003-IB6455	20031224
WO 2004058139	A3	20041104		

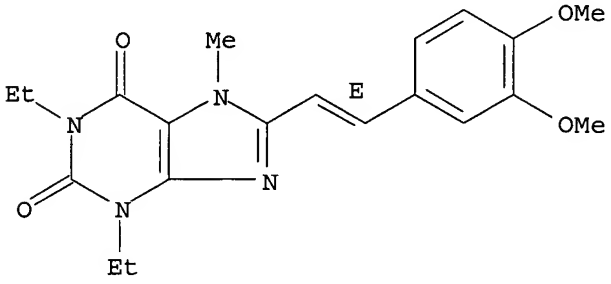
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-509039P P 20021227

AB The invention provides a method of treating behavioral disorders such as attention deficit hyperactivity disorder, comprising administering an effective amount of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine or a pharmaceutically acceptable salt to a patient. This method may also

be used for Tic/Tourette's disorder.
IC ICM A61K
CC 1-11 (Pharmacology)
IT **Brain**, disease
(Gilles de la Tourette syndrome, tic/Tourette's disorder; xanthine derivative for treatment of behavioral disorders)
IT **155270-99-8**
RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)
IT **155270-99-8**
RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(xanthine derivative for treatment of behavioral disorders)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:522325 HCAPLUS
DOCUMENT NUMBER: 141:99592
TITLE: Adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease
AUTHOR(S): Ochi, M.; Shiozaki, S.; Kase, H.
CORPORATE SOURCE: Pharmaceutical Research Institute, Ltd, Kyowa Hakko Kogyo Co., Shizuoka, 411-8731, Japan
SOURCE: Neuroscience (Oxford, United Kingdom) (2004), 127(1), 223-231
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A target neuron of adenosine A2A receptor antagonists to exert anti-parkinsonian activities has been currently identified to be, at least in part, striatopallidal medium spiny neurons (MSNs). In the present study, we determine whether A2A receptor-mediated modulation is associated with changes in the release of GABA and glutamate in the substantia nigra pars reticulata (SNr), an output structure of the whole basal ganglia network, using in vivo microdialysis in a rat Parkinson's disease (PD) model. In 6-hydroxydopamine (OHDA)-lesioned rats compared with normal rats, basal extracellular GABA levels in the SNr show no change, whereas basal glutamate levels are significantly increased. Oral administration of the A2A receptor-selective antagonist E-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-

methyl-3,7-dihydro-1-H-purine-2,6-dion (KW-6002) to 6-OHDA-lesioned rats at 1 mg/kg caused a marked and sustained increase of GABA and glutamate levels in the SNr. The increase of nigral glutamate by KW-6002 was abolished by a kainic acid-induced lesion of the globus pallidus (GP) or subthalamic nucleus (STN) in 6-OHDA-lesioned rats, whereas the increase of nigral GABA was completely blocked by the GP-lesion but only partially blocked by the STN-lesion. These results indicate that changes in neurotransmitter release in the SNr brought about by KW-6002 are largely attributable to blockade of A2A receptor-mediated modulation of striatopallidal MSNs. Thus, these actions of KW-6002 on striatopallidal MSNs may be the main mechanism for ameliorating PD by A2A antagonists.

CC 1-11 (Pharmacology)

ST Parkinsonism **brain** GABA glutamate adenosine A2A KW6002

IT **Brain**
(substantia nigra, pars reticulata; adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

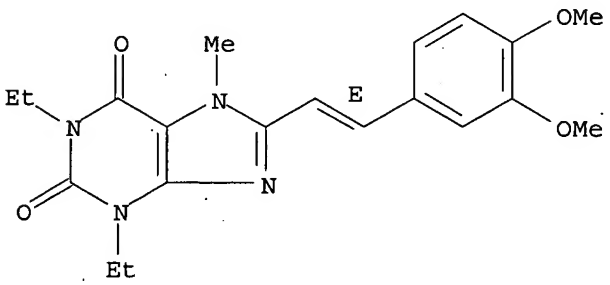
IT **155270-99-8**, KW-6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

IT **155270-99-8**, KW-6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(adenosine A2A receptor-mediated modulation of GABA and glutamate release in the output regions of the basal ganglia in a rodent model of Parkinson's disease)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004441787 EMBASE

TITLE: List of drugs in development for neurodegenerative diseases: Update June 2004.

AUTHOR: Kwon M.-O.; Fischer F.; Matthisson M.; Herrling P.

CORPORATE SOURCE: Prof. P. Herrling, Novartis International AG, Postfach,

CH-4002 Basel, Switzerland. Paul.Herrling@group.novartis.co
m
SOURCE: Neurodegenerative Diseases, (2004) Vol. 1, No. 2-3, pp.
113-152.
ISSN: 1660-2854 CODEN: NDEIA6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20050414
Last Updated on STN: 20050414

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

CT Medical Descriptors:
*degenerative disease: DT, drug therapy
drug effect
schizophrenia: DT, drug therapy
pain: DT, drug therapy
Alzheimer disease: DT, drug therapy
anxiety disorder: DT, drug therapy
psychosis: DT, drug therapy
sleep disorder: DT, drug therapy
major depression: DT, drug therapy
dementia: DT, drug therapy
schizoaffective psychosis: DT, drug therapy
Huntington chorea: DT, drug therapy
brain ischemia: DT, drug therapy
incontinence: DT, drug therapy
asthma: DT, drug therapy
central nervous system disease: DT, drug therapy
mental disease: DT, drug therapy
spinal cord injury: DT, drug therapy
brain disease: DT, drug therapy
attention deficit disorder: DT, drug therapy
epilepsy: DT, drug therapy
head injury: DT, drug therapy
liver cirrhosis: DT, drug therapy
cancer: DT, drug therapy
neuropathy: DT, drug therapy
multiple sclerosis: DT, drug therapy
neurotoxicity: DT, drug therapy
drug induced disease: DT, drug therapy
inflammation: DT, drug therapy
immune deficiency: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
chronic obstructive lung disease: DT, drug therapy
enteritis: DT, drug therapy
mood disorder: DT, drug therapy
coughing: DT, drug therapy
glaucoma: DT, drug therapy
motor neuron disease: DT, drug therapy
cognitive defect: DT, drug therapy
Parkinson disease: DT, drug therapy
migraine: DT, drug therapy
restenosis: DT, drug therapy
heart infarction: DT, drug therapy
autoimmune disease: DT, drug therapy

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respiratory distress syndrome: DT, drug therapy
systemic lupus erythematosus: DT, drug therapy
nervous system injury: DT, drug therapy
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senile arch: DT, drug therapy
prostate tumor: DT, drug therapy
drug mechanism
drug indication
human
review
priority journal
Drug Descriptors:
neuroleptic agent: DT, drug therapy
neuroleptic agent: PD, pharmacology
analgesic agent: DT, drug therapy
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nootropic agent: DT, drug therapy
nootropic agent: PD, pharmacology
neuroprotective agent: DT, drug therapy
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anticonvulsive agent: DT, drug therapy
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anxiolytic agent: DT, drug therapy
anxiolytic agent: PD, pharmacology
antineoplastic agent: DT, drug therapy
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muscle relaxant agent: DT, drug therapy
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monoamine oxidase B inhibitor: PD, pharmacology
adenosine kinase inhibitor: DT, drug therapy
adenosine kinase inhibitor: PD, pharmacology
dopamine 3 receptor blocking agent: DT, drug therapy
dopamine 3 receptor blocking agent: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
calpastatin: DT, drug therapy
calpastatin: PD, pharmacology

glycine receptor antagonist: DT, drug therapy
glycine receptor antagonist: PD, pharmacology
muscarinic M1 receptor agonist: DT, drug therapy
muscarinic M1 receptor agonist: PD, pharmacology
antiparkinson agent: DT, drug therapy
antiparkinson agent: PD, pharmacology
AMPA receptor antagonist: DT, drug therapy
AMPA receptor antagonist: PD, pharmacology
dopamine 2 receptor blocking agent: DT, drug therapy
dopamine 2 receptor blocking agent: PD, pharmacology
nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor: DT, drug therapy
nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase inhibitor: PD, pharmacology
unindexed drug
remacemide
selegiline

CT Drug Descriptors:

zydis
7b12
2 methyl 3 (2 pyrrolidinylmethoxy)pyridine
abs 205
a 72055
a 366833
a 35380
a 134974
ac 184897
ac 90222
6,7 dichloro 5 nitro 2,3 quinoxalinedione
acp 103
acpc
ad gl0002
aeg 3482
aeol 10150
agy 110
agy 207
ak 275
vasolex
alaptid
n (2 hydroxyethylamino) 3 nitronaphthalimide
altropane
am 36
donepezil
ampakines
Alzheimer disease vaccine
anatibant
apbpi 124
ar 139525
ar 15896
ar a 008055
spiro[1 azabicyclo[2.2.2]octane 3,2' thiazolidine] 2' one
ar r 18565
arry 142886
arx 2000
arx 2001
arx 2002
asenapine
aptiganel
as 600292

lanicemine
as 004509
as 601245
av 201
avp 923
recombinant ciliary neurotrophic factor
az 36041
azd 0328
ba 1016
bay 38 7271
bay x 9227
bd 1054
besonprodil
bgc 20 1178
1 (3,4 dihydroxy 5 nitrophenyl) 2 phenylethanone
bifeprunox
biii 890 cl
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide
bls 602
blonanserin
alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol
brasofensine
breflate
bls 605
bts 72664
bvt 2989
bxt 51072
cdd 0304
cee 03 310
cee 03 320
cep 1347
cep 3122
cep 4186
cep 751
cere 20
cere 130
cere 120
3 aminopropyl(diethoxymethyl)phosphinic acid
chf 2060
chf 3381
ckd 705
cnic 568
cns 2103
cns 5065
colostrinin
cp 132484
cp 283097
cp 465022
cpc 304
6 quinoxalinecarboxylic acid piperidide
dabelotine
dar 201
2 (2,3 dicarboxycyclopropyl)glycine
dd 20207
3,3 bis(3 fluorophenyl) n methylpropylamine
delucemine
10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone
novasite

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dp 109
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ect ad
ect pd
norphenazone
ef 7412
egis 7444
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tsukubaenolide
eliprodil
eht 201
pentoxifylline
aloxistatin acid
eqa 00
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f 10981
f 2 ccg i
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fce·29642a
ersofermin
ascomycin
n (4 acetyl 1 piperazinyl) 4 fluorobenzamide
flindokalner
formobactin
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fr 210575
galdansetron
ganstigmine
liatermine
gke 841
glialines
throphix
gmc 1111
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gpi 1485
gr 1485
5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]
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gv 2400
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ifenprodil

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clk 1
it 657
kf 17329
pralmorelin
krp 199
krx 411
istradefylline
l 687306
3 amino 1 hydroxy 4 methyl 2 pyrrolidinone
5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid
l 701252
lamotrigine
lau 0501
lau 8080
lax 101
lentivector
leteprinim
liga 20
5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone
decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid
decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid
decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3 isoquinolinecarboxylic acid
ly 302427
ly 354006
2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid
ly 451395
ly 483518
m 40401
mcc 257
4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine
4 carboxymethylamino 5,7 dichloro 2 quinolinecarboxylic acid
3,4 dihydro 3,3 dimethylisoquinoline 2 oxide
mdl 102288
3 (2 carboxy 2 phenylethenyl) 4,6 dichloro 1h indole 2 carboxylic acid
5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one
[1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester
3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid
recombinant somatomedin C
mem 1003
pramipexole
mito 4509
mito 4565
2 (2 oxo 1 pyrrolidinyl) n (5,6,7,8 tetrahydro 2,3 dimethylfuro[2,3 b]quinolin 4 yl)acetamide
lactacystin beta lactone
icosapentaenoic acid ethyl ester
ms 153
mt 5
n 3393
nbi 30702
nc 531
2 [4 methoxy 3 (2 phenylethoxy)phenyl] n,n dipropylethylamine
neramexane

neublastin
neurocale
neurostrol
neurovex
clomethiazole
5 (2 chloro 1 hydroxyethyl) 4 methylthiazole
nnc 07 0775
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione
noggin
norleu
nox 700
3 amino 1,1 bis(3 fluorophenyl)butane
nps 846
nrt 115
ns 1209
ns 1608
ns 2330
ns 257
ns 377
ns 638
CT Drug Descriptors:
ns 649
nt 4
nt 5
nw 1048
nxd 5150
nxd 9062
4 [(tert butylimino)methyl] 1,3 benzenedisulfonate disodium n oxide
ono 2506
n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1
piperazineacetamide
org 24448
p 58
p 9939
pan 811
pbt 1
pd 132026
pd 148903
pd 150606
pd 159265
pd 90780
pdc 008 004
pe21
perzinfotel
pn 277
pn 401
pnu 87663
2 dipropylamino 5,6 dimethoxyindan
6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h
pyrimido[4,5 b]indole
pnu 157678
pnu 170413
pnu 177864
pol 255
ppi 368
pre 103
prs 211220
pti 777
pym 50018

pym 50028
qg 2283
qr 333
r 1485
r 1577
ren 1654
ren 1820
rg 1068
ri 820
rjr 1401
2 (3 pyridinyl)quinuclidine
ro 09 2210
geomatrix
rpr 104632
rs 100642
s 312 d
s 1746
7 dipropylamino 2,3,5,6,7,8 hexahydronaphtho[2,3 b]furan
s 14820
s 176251
s 34730 1
s 34730
s 18986
s 33113 1
s 33138
sarizotan
4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole
5 chloro n [4 methoxy 3 (1 piperazinyl)phenyl] 3 methyl 2
benzothiophenesulfonamide
n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4
quinolinecarboxamide
sca 136
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5
c]pyrimidine
sea 0400
semax
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate
siclofen
sgs 518
sja 6017
2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine
skf 74652
3 allyl 6 chloro 2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3
benzazepine
sl 340026
sl 65 0155
7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone
slv 314
slv 319
sm 13496
SNX 482
sp (v5.2)c
spc 9766
sph 1371
spm 914
spm 935
sr 57667
sra 333

ssr 125047
ssr 146977
ssr 180575
ssr 181507
ssr 482073
ssr 504734
sumanirole
5 [3 [4 (4 fluorophenyl) 1 piperazinyl]propyl] 1,4,5,6,7,8 hexahydro 8 hydroxy 1 methylpyrrolo[3,2 c]azepin 4 one
sun n8075
survivins
sirenade
sym 2207
1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol
abs 301
abs 302
abs 304
talampanel
talnetant
taltirelin
alpha amino 2,5 dihydro 5 oxo 4 isoxazolepropionic acid
tc 1734
tc 2559
tch 346
tgp 580
thurinex

CT Drug Descriptors:

tk 14
tp 20
traxoprodil
ts 011
21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione
2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol
ucm 3100
2 dipropylamino 5 methoxy 1 methyltetralin
uk 351666
uk 356464
uk 356297
v 2006
vp 025
vx 799
way 855
wib 63480 2
win 68100
win 69211
xaliprodene
y 931
ykp 1358
6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione
omega conotoxin MVIIA
zonampanel
zt 1
fluoratec
ladostigil
hypophysis adenylate cyclase activating polypeptide

RN (muscle relaxant agent) 9008-44-0; (calpastatin) 79079-11-1; (remacemide) 111686-79-4; (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (2

methyl 3 (2 pyrrolidinylmethoxy)pyridine) 161417-03-4; (6,7 dichloro 5 nitro 2,3 quinoxalinedione) 153504-81-5; (altropane) 127648-29-7; (donepezil) 120011-70-3, 120014-06-4, 142057-77-0; (asenapine) 85650-56-2; (aptiganel) 137159-92-3, 137160-11-3; (lanicemine) 153322-05-5; (bifeprunox) 350992-10-8; (2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 134296-40-5; (blonanserin) 132810-10-7; (alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol) 99931-60-9; (brasofensine) 171655-91-7, 171655-92-8, 173830-18-7, 173830-20-1; (cep 1347) 156177-65-0, 170587-65-2; (cep 751) 156177-59-2, 199280-60-9; (3 aminopropyl(diethoxymethyl)phosphinic acid) 123690-79-9; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (3,3 bis(3 fluorophenyl) n methylpropylamine) 186495-99-8; (10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone) 160588-45-4; (norphenazone) 89-25-8; (tsukubaenolide) 104987-11-3; (eliprodil) 119431-25-3, 127293-58-7, 136634-88-3; (pentoxifylline) 6493-05-6; (aloxistatin acid) 76684-89-4; (ascomycin) 104987-12-4; (n (4 acetyl 1 piperazinyl) 4 fluorobenzamide) 133920-70-4; (5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]) 133156-06-6; (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (ifenprodil) 23210-56-2; (ipenoxazone) 104454-71-9; (pralmorelin) 158861-67-7; (istradefylline) **155270-99-8**; (3 amino 1 hydroxy 4 methyl 2 pyrrolidinone) 130931-65-6; (5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid) 139051-78-8; (lamotrigine) 84057-84-1; (leteprinim) 138117-50-7, 192564-13-9; (5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone) 107889-32-7; (decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid) 136845-59-5; (decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid) 136109-04-1, 137433-06-8; (decahydro 6 [2 (1h tetrazol 5 yl)ethyl] 3 isoquinolinecarboxylic acid) 154652-83-2; (2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid) 176199-48-7; (4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine) 109348-38-1, 135991-48-9, 99487-25-9; (3 (2 carboxy 2 phenylethenyl) 4,6 dichloro 1h indole 2 carboxylic acid) 161230-88-2; (5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one) 116114-14-8; ([1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester) 88191-84-8; (3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid) 130798-51-5; (pramipexole) 104632-26-0; (2 (2 oxo 1 pyrrolidinyl) n (5,6,7,8 tetrahydro 2,3 dimethylfuro[2,3 b]quinolin 4 yl)acetamide) 135463-81-9; (lactacystin beta lactone) 154226-60-5; (icosapentaenoic acid ethyl ester) 73310-10-8; (2 [4 methoxy 3 (2 phenylethoxy)phenyl] n,n dipropylethylamine) 149409-57-4; (clomethiazole) 1867-58-9, 533-45-9; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (4 [(tert butylimino)methyl] 1,3 benzenedisulfonate disodium n oxide) 168021-79-2; (n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide) 103233-65-4; (2 dipropylamino 5,6 dimethoxyindan) 82668-33-5; (6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole) 172035-74-4; (7 dipropylamino 2,3,5,6,7,8 hexahydronaphtho[2,3 b]furan) 121454-18-0, 157622-55-4, 172549-26-7; (4 (4 fluorophenyl) 2 (4 methylsulfinylphenyl) 5 (4 pyridyl)imidazole) 152121-47-6; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol) 191611-76-4; (3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate) 179120-52-6; (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4; (3 allyl 6 chloro 2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 80751-65-1; (7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone) 269718-83-4, 269718-84-5; (1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol) 142935-03-3; (talampanel) 161832-65-1, 161832-67-3; (talnetant)

174636-32-9, 204519-66-4; (taltirelin) 103300-74-9; (alpha amino 2,5 dihydro 5 oxo 4 isoxazolepropionic acid) 127607-88-9; (21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione) 110101-65-0; (2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol) 132535-61-6, 133681-84-2; (2 dipropylamino 5 methoxy 1 methyltetralin) 95999-11-4; (6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione) 143151-35-3, 154164-30-4; (omega conotoxin MVIIA) 107452-89-1; (hypophysis adenylate cyclase activating polypeptide) 137061-48-4

CN (1) Remacemide; (2) Selegiline; (3) Zydis; (4) 7b12; (5) Abt 089; (6) Abs 205; (7) A 72055; (8) A 366833; (9) A 35380; (10) A 134974; (11) Ac 184897; (12) Ac 90222; (13) Acea 1021; (14) Acp 103; (15) Acpc; (16) Ad gl0002; (17) Aeg 3482; (18) Aeol 10150; (19) Agy 110; (20) Agy 207; (21) Ak 275; (22) Vasolex; (23) Alaptid; (24) Ale 0540; (25) Altropane; (26) Am 36; (27) Aricept; (28) Ampakines; (29) An 1792; (30) Anatibant; (31) Apbpi 124; (32) Ar 139525; (33) Ar 15896; (34) Ar a 008055; (35) Ar r 17779; (36) Ar r 18565; (37) Arry 142886; (38) Arx 2000; (39) Arx 2001; (40) Arx 2002; (41) Asenapine; (42) Aptiganel; (43) As 600292; (44) Lanicemine; (45) As 004509; (46) As 601245; (47) Av 201; (48) Avp 923; (49) Axokine; (50) Az 36041; (51) Azd 0328; (52) Ba 1016; (53) Bay 38 7271; (54) Bay x 9227; (55) Bd 1054; (56) Besonprodil; (57) Bgc 20 1178; (58) Bia 3 202; (59) Bifeprunox; (60) Biii 890 cl; (61) Bimu 8; (62) Bls 602; (63) Blonanserin; (64) Bms 181100; (65) Brasofensine; (66) Breflate; (67) Bls 605; (68) Bts 72664; (69) Bvt 2989; (70) Bxt 51072; (71) Cdd 0304; (72) Cee 03 310; (73) Cee 03 320; (74) Cep 1347; (75) Cep 3122; (76) Cep 4186; (77) Cep 4186; (78) Cep 751; (79) Cere 20; (80) Cere 130; (81) Cere 120; (82) Cgp 35348; (83) Chf 2060; (84) Chf 3381; (85) Ckd 705; (86) Cnic 568; (87) Cns 2103; (88) Cns 5065; (89) Colostrinin; (90) Cp 132484; (91) Cp 283097; (92) Cp 465022; (93) Cpc 304; (94) Cx 516; (95) Dabelotine; (96) Dar 201; (97) DCG IV; (98) Dd 20207; (99) Nps 1506; (100) Delucemine; (101) Dmp 543; (102) Novasite; (103) Dp 103; (104) Dp 109; (105) Dp b99; (106) Dpp 225; (107) Dr 2313; (108) Dy 9760c; (109) E 2007; (110) E 2051; (111) E 2101; (112) Eaa 494; (113) Midafotel; (114) Eab 318; (115) Ect ad; (116) Ect pd; (117) Edaravone; (118) Ef 7412; (119) Egis 7444; (120) Eht 202; (121) Fk 506; (122) Eliprodil; (123) Eht 201; (124) Pentoxyfyllin; (125) Ep 475; (126) Eqa 00; (127) Anapsos; (128) Es 242 1; (129) F 10981; (130) F 2 ccg i; (131) Fce 29484a; (132) Fce 29642a; (133) Ersofermin; (134) Fk 520; (135) Fk 960; (136) Flindokalner; (137) Formobactin; (138) Fpl 16283; (139) Fr 210575; (140) Galdansetron; (141) Ganstigmine; (142) Liatermine; (143) Gke 841; (144) Glialines; (145) Throphix; (146) Gmc 1111; (147) Gp 14683; (148) Gpi 1485; (149) Gpi 1485; (150) Gr 1485; (151) Gr 73632; (152) Gt 2342; (153) Gt 715; (154) Gv 2400; (155) Gyki 52466; (156) Hf 0220; (157) Hp 184; (158) Ica 69673; (159) Idn 6556; (160) Ifenprodil; (161) Igt 440103; (162) Ino 1001; (163) Ipenoxazone; (164) Isp 1; (165) Clk 1; (166) It 657; (167) Kf 17329; (168) Kp 102; (169) Krp 199; (170) Krx 411; (171) Kw 6002; (172) L 687306; (173) L 687414; (174) L 689560; (175) L 701252; (176) Lamictal; (177) Lau 0501; (178) Lau 8080; (179) Lax 101; (180) Lentivector; (181) Leteprinim; (182) Liga 20; (183) Ly 178002; (184) Ly 233536; (185) Ly 274614; (186) Ly 293558; (187) Ly 302427; (188) Ly 354006; (189) Ly 354740; (190) Ly 451395; (191) Ly 483518; (192) M 40401; (193) Mcc 257; (194) Mci 225; (195) Mdl 100748; (196) Mdl 101002; (197) Mdl 102288; (198) Mdl 105519; (199) Mdl 27266; (200) Mdl 28170; (201) Mdl 29951; (202) Mecasermin; (203) Mem 1003; (204) Mem 1003; (205) Mirapex; (206) Mirapex; (207) Mito 4509; (208) Mito 4565; (209) Mkc 231; (210) Mln 519; (211) Mnd 21; (212) Ms 153; (213) Mt 5; (214) N 3393; (215) Nbi 30702; (216) Nc 531; (217) Ne 100; (218) Neotrofin; (219) Neramexane; (220) Neublastin; (221) Neurocale; (222) Neurostrol; (223) Neurovex; (224) Zendra; (225) Nla 715; (226) Nnc 07

0775; (227) Nnc 07 9202; (228) Noggin; (229) Norleu; (230) Nox 700
CN (231) Nps 1407; (232) Nps 846; (233) Nrt 115; (234) Ns 1209; (235) Ns 1608; (236) Ns 2330; (237) Ns 257; (238) Ns 377; (239) Ns 638; (240) Ns 649; (241) Nt 4; (242) Nt 5; (243) Nt 4; (244) Nt 5; (245) Nw 1048; (246) Nxd 5150; (247) Nxd 9062; (248) Nxy 059; (249) Nxy 059; (250) Ono 2506; (251) Opc 14117; (252) Org 24448; (253) P 58; (254) P 9939; (255) Pan 811; (256) Pbt 1; (257) Pd 132026; (258) Pd 148903; (259) Pd 150606; (260) Pd 159265; (261) Pd 90780; (262) Pdc 008 004; (263) Pe21; (264) Perzinfotel; (265) Pn 277; (266) Pn 401; (267) Pnu 87663; (268) Pnu 99194a; (269) Pnu 101033e; (270) Pnu 157678; (271) Pnu 170413; (272) Pnu 177864; (273) Pol 255; (274) Ppi 368; (275) Pre 103; (276) Prs 211220; (277) Pti 777; (278) Pym 50018; (279) Pym 50028; (280) Qg 2283; (281) Qr 333; (282) R 1485; (283) R 1577; (284) Ren 1654; (285) Ren 1820; (286) Rg 1068; (287) Ri 820; (288) Rjr 1401; (289) Rjr 2429; (290) Ro 09 2210; (291) Geomatrix; (292) Rpr 104632; (293) Rs 100642; (294) S 312 d; (295) S 1746; (296) S 14297; (297) S 14820; (298) S 176251; (299) S 34730 1; (300) S 34730; (301) S 18986; (302) S 33113 1; (303) S 33138; (304) Sarizotan; (305) Sb 203580; (306) Sb 271046; (307) Sb 277011; (308) Sca 136; (309) Sch 58261; (310) Sea 0400; (311) Semax; (312) Sib 1553a; (313) Sib 1765f; (314) Siclofen; (315) Sgs 518; (316) Sja 6017; (317) Skf 38393; (318) Skf 74652; (319) Skf 82958; (320) Sl 340026; (321) Sl 65 0155; (322) Slv 308; (323) Slv 314; (324) Slv 319; (325) Sm 13496; (326) SNX 482; (327) Sp (v5.2)c; (328) Spc 9766; (329) Sph 1371; (330) Spm 914; (331) Spm 935; (332) Sr 57667; (333) Sra 333; (334) Ssr 125047; (335) Ssr 146977; (336) Ssr 180575; (337) Ssr 181507; (338) Ssr 482073; (339) Ssr 504734; (340) Sumanirole; (341) Sun c5174; (342) Sun n8075; (343) Sun n8075; (344) Survivins; (345) Sirenade; (346) Sym 2207; (347) T 588; (348) Abs 301; (349) Abs 302; (350) Abs 304; (351) Talampanel; (352) Talampanel; (353) Talnetant; (354) Taltirelin; (355) Tan 950 a; (356) Tc 1734; (357) Tc 2559; (358) Tch 346; (359) Tgp 580; (360) Thurinex; (361) Tk 14; (362) Tp 20; (363) Traxoprodil; (364) Ts 011; (365) U 74500a; (366) U 78517f; (367) Ucm 3100; (368) Uh 232; (369) Uk 351666; (370) Uk 356464; (371) Uk 356297; (372) V 2006; (373) Vp 025; (374) Vx 799; (375) Vx 799; (376) Way 855; (377) Way 855; (378) Wib 63480 2; (379) Win 68100; (380) Win 69211; (381) Xaliprodene; (382) Y 931; (383) Ykp 1358; (384) Ym 90k; (385) Ziconotide; (386) Zonampanel; (387) Zt 1; (388) Ak 275; (389) Vasolex; (390) Fluoratec; (391) Ladostigil; (392) Liga 20; (393) PACAP; (394) Ampakines; (395) Ampakines; (396) Ampakines; (397) Apbpi 124

CO (3) Cardinal Health; (10) Abbott; (13) Cocensys novartis; (14) Acadia; (16) Actinodrug; (17) Aegera therapeutics; (18) Aeolus; (20) Agy therapeutics; (23) VUFB; (26) Amrad; (30) Fournier; (32) Arena; (37) Array biopharma; (40) Alpharx; (42) Oregon health sciences university; (47) Avigen; (48) Center for neurologic study; (50) Asahi Kasei; (52) Bioaxone; (55) Russian academy medical science; (56) Purdue neuroscience; (57) Sankyo; (58) Bial; (63) Dainippon; (66) Pharm eco; (67) Boston Life Sciences; (68) Knoll; (69) Biovitrum; (70) Oxis; (71) Cognitive; (77) Leo; (79) Stem cells

CO (80) The salk institute for biological studies; (81) University of washington; (85) Chong Kun Dang; (86) Cogent neuroscience; (88) CeNeS; (89) Regen; (93) Questcor; (96) Darpharma; (98) Diverdrugs; (100) NPS Pharmaceuticals; (105) D Pharm; (107) Meiji Seika Kaisha; (111) Eisai; (112) Btg novartis; (124) Exonhit therapeutics; (125) University of tennessee memphis; (127) Asac; (129) Fabre; (130) Tokyo metropolitan institute; (134) Kosan; (137) Kirin; (138) Fisons; (139) Fujisawa; (141) Chiesi; (142) Amgen; (143) Viatra viatris; (147) Sicor; (148) Guilford; (149) Symphony neuro development; (152) Gliatech; (153) GBtherapeutics; (154) BTG; (155) Egis; (156) Hunter Fleming; (158) Icagen; (159) Idun; (162) Inotek; (163) Nippon Chemiphar; (165) Chronogen; (166) Bristol Myers Squibb; (168) Krenitsky; (169) Kyorin; (170) Keryx; (171) Kyowa Hakko

Kogyo; (175) Merck and Co; (177) Louisiana university; (178) Louisiana state university; (179) Scotia holdings; (180) Oxford; (181) Spectrum; (182) Fidia; (192) Metaphore; (201) Hoechst Marion Roussel; (202) Cephalon; (203) Bayer; (204) Memory Pharmaceuticals; (206) Boehringer; (208) MitoKor; (210) PAION; (211) Mochida; (212) Mitsui; (214) Nisshin; (216) Neurochem; (218) NeoTherapeutics; (219) Merz; (220) Nsgene; (221) Apollo; (222) Neurocal; (223) Biovex; (227) Novo Nordisk; (228) Regeneron; (229) Hedral therapeutics; (230) Medinox; (232) Nps; (240) Neurosearch; (242) Genentech; (244) Ceregene; (245) Newron; (247) Nymox; (250) Ono; (251) Otsuka; (254) Aventis; (255) Panacea; (256) Prana Biotechnology; (261) Parke Davis; (262) Pharmaceutical Discovery; (263) Inserm; (265) Proneuron biotechnologies; (266) Wellstat Therapeutics; (272) Pharmacia; (273) Polifarma; (274) Praecis; (275) Prescient neuropharma; (276) Pharmos; (277) Proteotech; (279) Phytopharm; (280) Quark biotech; (281) Quigley; (284) Centaur; (285) Reneuron; (286) Repligen; (287) Rinat neuroscience; (289) Reynolds Tobacco; (292) Rhone Poulenc Rorer; (293) Hoffmann La Roche; (295) Shionogi; (303) Servier; (304) Merck AG; (311) Russian Academy of Sciences; (313) Sibia; (314) Schering Plough; (316) Senju; (318) Glaxo SmithKline; (320) Synthelabo; (324) Solvay; (325) Sumitomo

CO (327) Supratek; (328) Celgene; (329) Sanochemia; (330) Alviva biopharmaceuticals; (331) Albert ludwigs; (342) Daiichi Seiyaku; (343) Suntory; (344) Allelix; (345) Polichem; (346) Annovis; (347) Toyama; (350) American Biogenetic Sciences; (351) Lilly; (352) Ivax; (353) SmithKline Beecham; (354) Tanabe Seiyaku; (357) Targacept; (358) Novartis; (359) Takeda; (360) Thuris; (361) Lonza; (362) AVANT; (364) Taisho; (366) Pharmacia Upjohn; (367) Universidad complutense de madrid; (368) Astra; (371) Pfizer; (372) Vernalis; (373) Vasogen; (374) Serono; (375) Vertex; (376) Neurocrine Biosciences; (380) Sterling Winthrop; (381) Sanofi Synthelabo; (382) Mitsubishi; (383) Sk; (385) Elan; (386) Yamanouchi; (387) Shanghai Institute of Materia Medica; (389) Alkermes; (390) Harvard university; (391) Hebrew university of jerusalem; (392) Georgetown institute for neurosciences; (393) Tulane University; (394) University of California; (395) Cortex; (396) Organon; (397) Wyeth; Fujimoto seiyaku; Carlbiotech; National Institute of Health; 4sc; Merck Sharp and Dohme; Sigma Tau; Ferrer; Synaptica; Isis; Pharmexa; Axonyx; Paracelsian; Britannia; Immunogen; GE Medical Systems; Acorda; Biocryst; Sunesis; Pfizer pharmacia; National institute of aging

CO Searle; Titan; Ryan; Nimh; Maas biolab; Pierre fabre reckitt and coleman; Purdue; Societe Misr Pour l'Industrie Pharmaceutique; Organix; Korea Research Institute; Juvantia; Oxford BioMedica; Glaxo Wellcome; Janssen; American Cyanamid; Curis; Tapestry; Acgera therapeutics; Ortho; Cytos Biotechnology; Ncrr; Yeda research; Research Triangle Institute; Renovis; Forest; Pharmed Private; Pharmacyclics; Sibia neuroscience; MERA; Toray; Tuszynski; Ucsd; Neurospheres; Beaufour; Johnson and Johnson; Lifegroup; Cellfactors; Alexion; University of nottingham; Richter; Teva; Asta; Aderis; Biofrontera; Sagami; Bresagen; Digital gene technologies; Novavax; Royal gist brocades; Us national institute on drug abuse; University of South Florida; University of pennsylvania; University of Georgetown; Samaritan; University of queensland; University of Oregon; Memorial sloan kettering cancer center; University of Chicago; Johns hopkins university; Hokkaido University; University of florence; Universita di sienna; University of kuopio; Finncovery

L34 ANSWER 7 OF 40 EMBASE
on STN

ACCESSION NUMBER: 2004198619 EMBASE

TITLE: List of drugs in development for neurodegenerative diseases.

AUTHOR: Fischer F.; Matthisson M.; Herrling P.
CORPORATE SOURCE: Prof. P. Herrling, Novartis International AG, Postfach, CH-4002 Basel, Switzerland. Paul.Herrling@group.novartis.com
SOURCE: Neurodegenerative Diseases, (2004) Vol. 1, No. 1, pp. 50-70.
ISSN: 1660-2854 CODEN: NDEIA6
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 20050414
Last Updated on STN: 20050414

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

CT Medical Descriptors:
*degenerative disease: DT, drug therapy
Huntington chorea: DT, drug therapy
brain ischemia: DT, drug therapy
Parkinson disease: DT, drug therapy
epilepsy: DT, drug therapy
anxiety disorder: DT, drug therapy
schizophrenia: DT, drug therapy
pain: DT, drug therapy
Alzheimer disease: DT, drug therapy
spinal cord injury: DT, drug therapy
brain injury: DT, drug therapy
immune deficiency: DT, drug therapy
chronic obstructive lung disease: DT, drug therapy
enteritis: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
human
clinical trial
article
priority journal
Drug Descriptors:
remacemide: DV, drug development
remacemide: DT, drug therapy
remacemide: PD, pharmacology
selegiline: CT, clinical trial
selegiline: DT, drug therapy
selegiline: PD, pharmacology
adenosine kinase inhibitor: DV, drug development
adenosine kinase inhibitor: DT, drug therapy
adenosine kinase inhibitor: PD, pharmacology
nicotinic agent: DV, drug development
nicotinic agent: DT, drug therapy
nicotinic agent: PD, pharmacology
muscarinic agent: DV, drug development
muscarinic agent: DT, drug therapy
muscarinic agent: PD, pharmacology
nootropic agent: CT, clinical trial
nootropic agent: DT, drug therapy
nootropic agent: PD, pharmacology
calpastatin: DV, drug development
calpastatin: DT, drug therapy
calpastatin: PD, pharmacology
AMPA receptor antagonist: DV, drug development

AMPA receptor antagonist: DT, drug therapy
AMPA receptor antagonist: PD, pharmacology
n methyl dextro aspartic acid receptor blocking agent: DV, drug development
n methyl dextro aspartic acid receptor blocking agent: DT, drug therapy
n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
4 aminobutyric acid A receptor stimulating agent: DV, drug development
4 aminobutyric acid A receptor stimulating agent: DT, drug therapy
4 aminobutyric acid A receptor stimulating agent: PD, pharmacology
calcium channel blocking agent: DV, drug development
calcium channel blocking agent: DT, drug therapy
calcium channel blocking agent: PD, pharmacology
immunomodulating agent: CT, clinical trial
immunomodulating agent: DT, drug therapy
immunomodulating agent: PD, pharmacology
cholinesterase inhibitor: CT, clinical trial
cholinesterase inhibitor: DT, drug therapy
cholinesterase inhibitor: PD, pharmacology
serotonin agonist: DV, drug development
serotonin agonist: DT, drug therapy
serotonin agonist: PD, pharmacology
adrenergic receptor stimulating agent: DV, drug development
adrenergic receptor stimulating agent: DT, drug therapy
adrenergic receptor stimulating agent: PD, pharmacology
glutamate receptor agonist: DV, drug development
glutamate receptor agonist: DT, drug therapy
glutamate receptor agonist: PD, pharmacology
antioxidant: DV, drug development
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
alpha 2 adrenergic receptor blocking agent: CT, clinical trial
alpha 2 adrenergic receptor blocking agent: DT, drug therapy
alpha 2 adrenergic receptor blocking agent: PD, pharmacology
chelating agent: DV, drug development
chelating agent: DT, drug therapy
chelating agent: PD, pharmacology
serotonin 1A antagonist: CT, clinical trial
serotonin 1A antagonist: DT, drug therapy
serotonin 1A antagonist: PD, pharmacology
scavenger: DV, drug development
scavenger: DT, drug therapy
scavenger: PD, pharmacology
serotonin 3 antagonist: DV, drug development
serotonin 3 antagonist: DT, drug therapy
serotonin 3 antagonist: PD, pharmacology
glycine receptor antagonist: DV, drug development
glycine receptor antagonist: DT, drug therapy
glycine receptor antagonist: PD, pharmacology
potassium channel stimulating agent: CT, clinical trial
potassium channel stimulating agent: DT, drug therapy
potassium channel stimulating agent: PD, pharmacology
ionotropic receptor agonist: CT, clinical trial
ionotropic receptor agonist: DT, drug therapy
ionotropic receptor agonist: PD, pharmacology
caspase inhibitor: DV, drug development
caspase inhibitor: DT, drug therapy
caspase inhibitor: PD, pharmacology
muscarinic M1 receptor agonist: DV, drug development
muscarinic M1 receptor agonist: DT, drug therapy

muscarinic M1 receptor agonist: PD, pharmacology
monoamine oxidase B inhibitor: DV, drug development
monoamine oxidase B inhibitor: DT, drug therapy
monoamine oxidase B inhibitor: PD, pharmacology
cysteine proteinase inhibitor: DV, drug development
cysteine proteinase inhibitor: DT, drug therapy
cysteine proteinase inhibitor: PD, pharmacology
unindexed drug
a 134974
a 366833
a 35380
a 72055
abs 205
ac 184897
ac 90222
6,7 dichloro 5 nitro 2,3 quinoxalinedione
aeg 3482
CT Drug Descriptors:
agy 110
agy 207
ak 275
n (2 hydroxyethylamino) 3 nitronaphthalimide
am 36
Alzheimer disease vaccine
apbpi 124
ar 139525
ar 15896
ar a 008055
spiro[1 azabicyclo[2.2.2]octane 3,2' thiazolidine] 2' one
ar r18565
arry 142886
arx 2000
as 600292
as 004509
as 601245
az 36041
ba 1016
bay x 9227
bd 1054
bgc 20 1178
bls 602
bls 605
2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide
alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol
cas 493
cep 1347
cep 4143
cep 3122
cep 4186
cep 751
cere 20
3 aminopropyl(diethoxymethyl)phosphinic acid
chf 2060
cnic 568
cns 1044
cns 2103
cns 5065
cp 132484

cp 283097
cpc 304
6 quinoxalinecarboxylic acid piperidide
2 (2,3 dicarboxycyclopropyl)glycine
dd 20207
10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone
dp 103
dp 109
dp b99
dpp 225
e 2101
eaa 404
eab 318
ef 7412
egis 7444
eht 202
aloxistatin acid
eqa 00
es 2421
f 10981
f 2 ccg 1
fce 29484 a
fibroblast growth factor 9
fpl 16283
ggf 2
gke 841
gp 14683
gpi 1337
gpi 1485
5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]
4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1
piperazinecarboxylic acid methyl ester
gt 2342
gt 715
gv 2400
1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine
hf 0220
hp 184
idn 6556
clk 1
isp 1
kf 17329
pralmorelin
krx 411
istradefylline
l 687306
3 amino 1 hydroxy 4 methyl 2 pyrrolidinone
5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic
acid
l 701252
lau 0501
liga 20
5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone
decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid
decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid
ly 302427
ly 354006
2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid
ly 451395

mcc 257
4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine
4 carboxymethylamino 5,7 dichloro 2 quinolinecarboxylic acid
3,4 dihydro 3,3 dimethylisoquinoline 2 oxide
mdl 102288
5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one
[1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester
3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid
mem 1003
lactacystin beta lactone
ms 153
mt 5
n 3393
nbi 30702
nc 531
5 (2 chloro 1 hydroxyethyl) 4 methylthiazole
nnc 070775
nnc 079202
nox 700

CT Drug Descriptors:

3 amino 1,1 bis(3 fluorophenyl)butane
nps 846
nrt 115
ns 1209
ns 1608
ns 257
ns 377
ns 638
ns 649
nxd 5150
nyx 059
ono 2506
n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide
p 58
p 9939
pan 811
pbt 1
pd 132026
pd 150606
pd 159265
pd 90780
pdc 008004
n sec butyl 1 (2 chlorophenyl) n methyl 3 isoquinolinecarboxamide
pn 277
6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole
pnu 157678
pnu 87663
pol 255
ppi 368
pre 368
prs 211220
pym 50028
qg 2283
ren 1654
ren 1820
ri 820

rjr 1401
ro 092210
rpr 104632
rs 100642
s 14820
s 176251
s 34730 1
s 18986
s 312 d
s 33113 1
5 chloro n [4 methoxy 3 (1 piperazinyl)phenyl] 3 methyl 2 benzothiophenesulfonamide
n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate
sja 6017
skf 74652
sl 340026
7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone
SNX 482
spc 9766
sph 1371
spm 914
spm 935
ssr 180575
ssr 482073
5 [3 [4 (4 fluorophenyl) 1 piperazinyl]propyl] 1,4,5,6,7,8 hexahydro 8 hydroxy 1 methylpyrrolo[3,2 c]azepin 4 one
sym 2207
1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol
abs 301
abs 302
abs 304
tan 950a
tc 2559
tch 346
tgp 580
tk 14
tp 20
21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione
2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol
uk 351666
uk 356464
uk 356297
vx 799
way 855
wib 63480 2
win 67500
win 68100
win 69211
6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione

RN (remacemide) 111686-79-4; (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (calpastatin) 79079-11-1; (6,7 dichloro 5 nitro 2,3 quinoxalinedione) 153504-81-5; (2,3 dihydro 3 isopropyl 2 oxo 1 benzimidazolecarboxylic acid 3alpha tropanylamide) 134296-40-5; (alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol) 99931-60-9;

(cep 1347) 156177-65-0, 170587-65-2; (cep 751) 156177-59-2, 199280-60-9; (3 aminopropyl(diethoxymethyl)phosphinic acid) 123690-79-9; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (10,10 bis(2 fluoro 4 pyridinylmethyl) 9(10h) anthracenone) 160588-45-4; (aloxistatin acid) 76684-89-4; (fibroblast growth factor 9) 151185-16-9; (5 aminovalerylsubstance P [7-11][9 proline 10 (n methylleucine)]) 133156-06-6; (4 [(3,4 dichlorophenyl)acetyl] 3 (1 pyrrolidinylmethyl) 1 piperazinecarboxylic acid methyl ester) 126766-32-3; (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (pralmorelin) 158861-67-7; (istradefylline) **155270-99-8**; (3 amino 1 hydroxy 4 methyl 2 pyrrolidinone) 130931-65-6; (5,7 dichloro 1,2,3,4 tetrahydro 4 (3 phenylureido) 2 quinolinecarboxylic acid) 139051-78-8; (5 (3,5 di tert butyl 4 hydroxybenzylidene) 4 thiazolidinone) 107889-32-7; (decahydro 6 (2h tetrazol 5 ylmethyl) 3 isoquinolinecarboxylic acid) 136845-59-5; (decahydro 6 phosphonomethyl 3 isoquinolinecarboxylic acid) 136109-04-1, 137433-06-8; (2 aminobicyclo[3.1.0]hexane 2,6 dicarboxylic acid) 176199-48-7; (4 (2 fluorophenyl) 6 methyl 2 (1 piperazinyl)thieno[2,3 d]pyrimidine) 109348-38-1, 135991-48-9, 99487-25-9; (5 (4 chlorophenyl) 4 ethyl 2,4 dihydro 2 methyl 3h 1,2,4 triazol 3 one) 116114-14-8; ([1 [(1 formyl 2 phenylethyl)carbamoyl] 2 methylpropyl]carbamic acid benzyl ester) 88191-84-8; (3 (2 carboxy 4,6 dichloro 3 indolyl)propionic acid) 130798-51-5; (lactacystin beta lactone) 154226-60-5; (n (7 hydroxy 2,2,4,6 tetramethyl 1 indanyl) 4 (3 methoxyphenyl) 1 piperazineacetamide) 103233-65-4; (n sec butyl 1 (2 chlorophenyl) n methyl 3 isoquinolinecarboxamide) 85532-75-8; (6,7,8,9 tetrahydro 9 (2 morpholinoethyl) 2,4 bis(1 pyrrolidinyl) 5h pyrimido[4,5 b]indole) 172035-74-4; (4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol) 191611-76-4; (3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine fumarate) 179120-52-6; (7 (4 methyl 1 piperazinyl) 2(3h) benzoxazolone) 269718-83-4, 269718-84-5; (1 (benzo[b]thien 5 yl) 2 (2 diethylaminoethoxy)ethanol) 142935-03-3; (21 [4 [5,6 bis(diethylamino) 2 pyridyl] 1 piperazinyl] 16alpha methylpregna 1,4,9(11) triene 3,20 dione) 110101-65-0; (2 [[4 [2,6 bis(1 pyrrolidinyl) 4 pyrimidinyl] 1 piperazinyl]methyl] 3,4 dihydro 2,5,7,8 tetramethyl 2h 1 benzopyran 6 ol) 132535-61-6, 133681-84-2; (6 (1 imidazolyl) 7 nitro 2,3 quinoxalinedione) 143151-35-3, 154164-30-4

CN (1) A 134974; (2) A 366833; (3) A 35380; (4) A 72055; (5) Abs 205; (6) Ac 184897; (7) Ac 90222; (8) Acea 1021; (9) Aeg 3482; (10) Agy 110; (11) Agy 207; (12) Ak 275; (13) Ak 275; (14) Ale 0540; (15) Am 36; (16) An 1792; (17) Apbpi 124; (18) Ar 139525; (19) Ar 15896; (20) Ar a 008055; (21) Ar r 17779; (22) Ar r18565; (23) Arry 142886; (24) Arx 2000; (25) As 600292; (26) As 004509; (27) As 601245; (28) Az 36041; (29) Ba 1016; (30) Bay x 9227; (31) Bd 1054; (32) Bgc 20 1178; (33) Bls 602; (34) Bls 605; (35) Bimu 8; (36) Bms 181100; (37) Cas 493; (38) Cep 1347; (39) Cep 4143; (40) Cep 3122; (41) Cep 4186; (42) Cep 751; (43) Cere 20; (44) Cgp 35348; (45) Chf 2060; (46) Cnic 568; (47) Cns 1044; (48) Cns 2103; (49) Cns 5065; (50) Cp 132484; (51) Cp 283097; (52) Cpc 304; (53) Cx 516; (54) DCG IV; (55) Dd 20207; (56) Dmp 543; (57) Dp 103; (58) Dp 109; (59) Dp b99; (60) Dpp 225; (61) E 2101; (62) Eaa 404; (63) Eab 318; (64) Ef 7412; (65) Egis 7444; (66) Eht 202; (67) Ep 475; (68) Eqa 00; (69) Es 2421; (70) F 10981; (71) F 2 ccg 1; (72) Fce 29484 a; (73) FGF 9; (74) Fpl 16283; (75) Ggf 2; (76) Gke 841; (77) Gp 14683; (78) Gpi 1337; (79) Gpi 1485; (80) Gr 73632; (81) Gr 89696; (82) Gt 2342; (83) Gt 715; (84) Gv 2400; (85) Gyki 52466; (86) Hf 0220; (87) Hp 184; (88) Idn 6556; (89) Clk 1; (90) Isp 1; (91) Kf 17329; (92) Kp 102; (93) Krx 411; (94) Kw 6002; (95) L 687306; (96) L 687414; (97) L 689560; (98) L 701252; (99) Lau 0501; (100) Liga 20; (101) Ly 178002; (102) Ly 233536; (103) Ly 235959; (104) Ly 274614; (105) Ly 302427; (106) Ly 354006; (107) Ly 354740; (108) Ly 451395; (109) Mcc 257; (110) Mci 225; (111) Mdl 100748; (112) Mdl 101002; (113) Mdl 102288; (114)

Mdl 27266; (115) Mdl 28170; (116) Mdl 29951; (117) Mem 1003; (118) Mln 519; (119) Ms 153; (120) Mt 5; (121) N 3393; (122) Nbi 30702; (123) Nc 531; (124) Nla 715; (125) Nnc 070775; (126) Nnc 079202; (127) Nox 700; (128) Nps 1407; (129) Nps 846; (130) Nrt 115; (131) Ns 1209; (132) Ns 1608; (133) Ns 257; (134) Ns 377; (135) Ns 638; (136) Ns 649; (137) Nxd 5150; (138) Nyx 059; (139) Ono 2506; (140) Opc 14117; (141) P 58; (142) P 9939; (143) Pan 811; (144) Pbt 1; (145) Pd 132026; (146) Pd 150606; (147) Pd 159265; (148) Pd 90780; (149) Pdc 008004; (150) Pk 11195; (151) Pn 277; (152) Pnu 101033e; (153) Pnu 157678; (154) Pnu 87663; (155) Pol 255; (156) Ppi 368; (157) Pre 368; (158) Prs 211220; (159) Pym 50028; (160) Qg 2283; (161) Ren 1654; (162) Ren 1820; (163) Ri 820; (164) Rjr 1401; (165) Ro 092210; (166) Rpr 104632; (167) Rs 100642; (168) S 14820; (169) S 176251; (170) S 34730 1; (171) S 18986; (172) S 312 d; (173) S 33113 1; (174) Sb 271046; (175) Sb 277011; (176) Sib 1553a; (177) Sib 1765f; (178) Sja 6017; (179) Skf 74652; (180) Sl 340026; (181) Slv 308; (182) SNX 482; (183) Spc 9766; (184) Sph 1371; (185) Spm 914; (186) Spm 935; (187) Ssr 180575; (188) Ssr 482073; (189) Sun c5174; (190) Sym 2207; (191) T 588; (192) Abs 301; (193) Abs 302; (194) Abs 304; (195) Tan 950a; (196) Tc 2559; (197) Tch 346; (198) Tgp 580; (199) Tk 14; (200) Tp 20; (201) U 74500a; (202) U 78517f; (203) Uk 351666; (204) Uk 356464; (205) Uk 356297; (206) Vx 799; (207) Way 855; (208) Wib 63480 2; (209) Win 67500; (210) Win 68100; (211) Win 69211; (212) Ym 90k

CO (4) Abbott; (7) Acadia; (8) Cocensys; (9) Aegera therapeutics; (11) Agy therapeutics; (13) Alkermes; (14) NPS Allelix; (15) Amrad; (17) Apollo

CO (18) Arena; (23) Array biopharma; (24) Alpharx; (28) Asahi Kasei; (29) Bioaxone therapeutique; (31) Russian academy of medical science; (32) Sankyo; (34) Boston Life Sciences; (35) Boehringer Ingelheim; (41) Leo; (42) Cephalon; (43) Stem cells; (45) Chiesi; (46) Cogent neuroscience; (52) Questcor; (53) Cortex; (55) Diverdrug; (56) Bristol Myers Squibb; (59) D Pharm; (61) Eisai; (63) Wyeth; (64) Universidad complutense de madrid; (66) Exonhit therapeutics; (67) University of tennessee memphis; (68) Asac; (70) Centre de reserche pierre fabre; (71) Tokyo metropolitan institute; (73) Amgen; (74) Fisons; (75) CeNeS; (76) Viatraviatris; (77) Sicor; (79) Guilford; (82) Gliatech; (83) GB; (84) BTG; (85) Egis; (86) Hunter Fleming; (88) Idun; (90) Chronogen; (92) Krenitsky; (93) Keryx; (94) Kyowa Hakko Kogyo; (98) Merck and Co; (99) Louisiana university; (100) Fidia; (108) Lilly; (110) Mitsubishi; (116) Hoechst Marion Roussel; (117) Bayer; (118) PAION; (119) Mitsui; (120) Taisho; (121) Nisshin; (122) Neurocrine bioscience; (123) Neurochem; (124) Astra Zeneca; (126) Novo Nordisk; (127) Medinox; (129) Nps; (136) Neurosearch; (137) Nymox; (139) Ono; (140) Otsuka; (142) Aventis; (143) Panacea; (144) Prana Biotechnology; (148) Parke Davis; (149) Pharmaceutical Discovery; (150) Universita di siena; (151) Proneuron biotechnologies; (155) Polifarma; (156) Praecis; (157) Prescient; (158) Pharmos; (159) Phytopharma; (160) Quark biotech; (161) Centaur; (162) Reneuron; (163) Rinat neuroscience; (164) Rj reynolds tobacco; (166) Rhone Poulenc Rorer; (167) Hoffmann La Roche; (172) Shionogi; (173) Servier; (177) Sibia; (178) Senju; (179) Glaxo SmithKline; (180) Synthelabo; (181) Solcvay; (182) Elan; (183) Celgene; (184) Sanochemia; (185) Alviva; (186) Albert ludwigs universitaet freiburg; (188) Sanofi Synthelabo; (189) Suntory; (190) Annovis; (191) Toyama; (194) American Biogenetic Sciences; (196) Targacept; (197) Novartis; (198) Takeda; (199) Lonza; (200) AVANT; (202) Pharmacia Upjohn; (205) Pfizer; (206) Serono; (207) Neurocrine Biosciences; (211) Sterling Winthrop; (212) Yamanouchi

CO Carlbiotech; Cardinal Health; University of South Florida; Fujimoto seiyaku; National Institute of Health; VUFB; University of California; Organon; Axonyx; Paracelsian; Immunogen; Oregon health sciences university; Pharmexa; Regeneron; Pharma eco; Ryan pharmaceuticals; Nimh; Maas biolab; Memorial sloankettering cancer center; Hebrew university;

Fabre; Schering; Societe Misr Pour l'Industrie Pharmaceutique; Korea research institute of bioscience and biotechnology; Knoll; National institute of aging; Searle; Kirin; Synaptica; Genentech; National institute of neurological disorders and stroke; American Cyanamid; Ncrr; Yeda research and development; Research Triangle Institute; Nippon Chemiphar; Spectrum; Merz; Pharmed Private; Pharmacyclics; MERA; Toray; NeoTherapeutics; Tuszynski; Nsgene; Neurocal; Hedral; Tulane University; Lifegroup; Inserm; Richter; Teva; Janssen; Newron; Russian Academy of Sciences; Schering Plough; Supratek; Ivax; Tanabe; Thuris; Us national institute drug abuse

L34 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610271 HCAPLUS
DOCUMENT NUMBER: 139:143978
TITLE: Methods using adenosine A2A receptor antagonists for treating Parkinson's disease patients suffering from L-DOPA/dopamine agonist therapy-associated movement disorders
INVENTOR(S): Kase, Hiroshi; Mori, Akihisa; Waki, Yutaka; Ohsawa, Yutaka; Karasawa, Akira; Kuwana, Yoshitoshi
PATENT ASSIGNEE(S): Japan
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063876	A2	20030807	WO 2003-US2658	20030128
WO 2003063876	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473864	AA	20030807	CA 2003-2473864	20030128
US 2004198753	A1	20041007	US 2003-353240	20030128
EP 1469855	A2	20041027	EP 2003-705971	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006919	A	20041109	BR 2003-6919	20030128
PRIORITY APPLN. INFO.:			US 2002-352413P P	20020128
			WO 2003-US2658 W	20030128

OTHER SOURCE(S): MARPAT 139:143978
AB The invention provides methods for treating movement disorders by administering an effective amount of one or more adenosine A2A receptor antagonist(s) to a patient in need thereof. The invention also provides methods of decreasing the adverse effects of L-DOPA in patients receiving L-DOPA therapy in the treatment of Parkinson's disease. The invention further provides methods and compns. for treating Parkinson's disease patients with sub-clin. EDs of L-DOPA by combining L-DOPA treatment with an effective amount of one or more adenosine A2A receptor antagonists (i.e.,

L-DOPA sparing effect). The invention further provides methods of effective treatment of Parkinson's disease by co-administering at least one adenosine A2A receptor antagonist, L-DOPA, and a dopamine agonist and/or a COMT inhibitor and/or a MAO inhibitor. The invention further provides methods of prolonging effective treatment of Parkinson's disease by administering an adenosine A2A receptor antagonist singly or together with a dopamine agonist, and/or a COMT inhibitor, and/or a MAO inhibitor without prior or subsequent administration of L-DOPA, delaying or removing onset of L-DOPA motor complication.

IC ICM A61K031-522
ICS A61P025-16

CC 1-11 (Pharmacology)

IT **Brain**
(substantia nigra, pars reticulata; adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

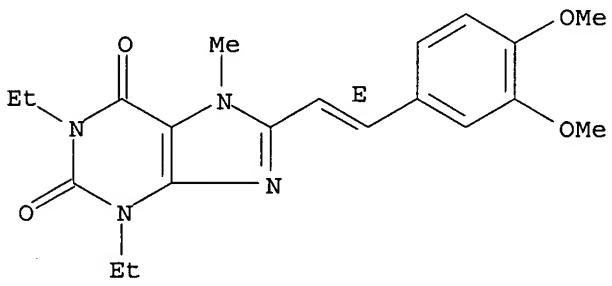
IT 69-89-6D, Xanthine, derivs. 322-35-0, Benserazide **155270-99-8**, KW 6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

IT **155270-99-8**, KW 6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2a antagonist for treating Parkinson's disease patients with L-DOPA/dopamine agonist therapy-associated motor complications)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:376384 HCAPLUS

DOCUMENT NUMBER: 138:396214

TITLE: Methods and compositions for reducing ischemic injury of the heart by administering adenosine receptor agonists and antagonists

INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of U.S. 6,211,165.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003092668	A1	20030515	US 2001-800274		20010305
US 6586413	B2	20030701			
US 6211165	B1	20010403	US 1999-423129		19991105
PRIORITY APPLN. INFO.:			US 1999-423129	A2	19991105
			US 1997-46030P	P	19970509
			US 1997-61716P	P	19971010
			WO 1998-US9031	W	19980508

AB Compns. and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment of the invention comprises the simultaneous administration of specific A3/A1 receptor agonists to patients suffering from ischemic damage or at risk for the same. In yet another embodiment of the invention, a binary conjugate which acts as an agonist for the A3 receptor and an antagonist at the A2a receptor, is administered to reduce or prevent ischemic damage to the heart.

IC ICM A61K031-7076
INCL 514046000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63

IT **Anti-ischemic agents**
Apoptosis
Drug interactions
Human
Signal transduction, biological
Surgery
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

IT **Ischemia**
(cardiac; adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

IT 14114-46-6, DMPX 31377-34-1 **31377-36-3 31377-40-9**
36396-99-3 37739-05-2 38594-96-6 41552-82-3 96760-69-9
103201-24-7 130714-47-5 139180-30-6, ZM241385 143668-15-9
147700-11-6, 8-(3-Chlorostyryl)caffeine 147700-48-9 148589-13-3
149744-74-1 150995-09-8 152918-18-8, IB-MECA 152918-28-0,
MRS 1340 152918-39-3 **158962-89-1** 160098-96-4, SCH58261
162684-35-7 163042-87-3, MRS 584 163042-96-4, Cl-IB-MECA
163152-33-8, MRS 537 163259-37-8, MRS 479 169190-74-3 170966-25-3
173845-91-5 173846-04-3, MRS 646 174365-19-6 193416-72-7
193416-77-2 193416-81-8 193416-84-1 193416-86-3 **193416-91-0**
193416-92-1 193416-94-3 193416-95-4 **193416-96-5**
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212687-47-3 212687-48-4 212687-49-5
212687-50-8 212687-51-9 212687-52-0
215933-83-8, MRS 580 215933-84-9, MRS 1364 215933-89-4 281191-56-8
281191-59-1 312488-51-0, MRS 1543 524699-43-2 524699-44-3
528853-03-4, MRS 1525
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

IT **31377-36-3 31377-40-9 149744-74-1**
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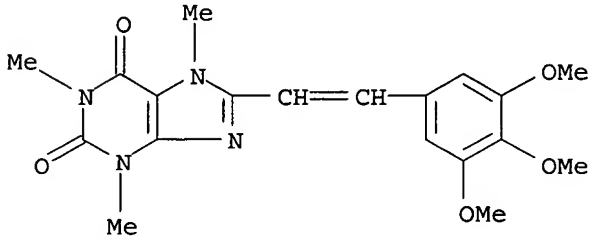
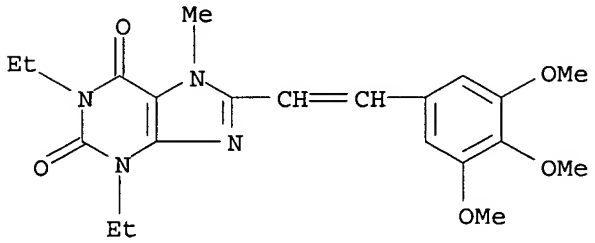
193416-97-6 212687-47-3 212687-48-4

212687-49-5 212687-50-8 212687-51-9
212687-52-0
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine receptor agonists and antagonists for reducing cardiac ischemic injury)

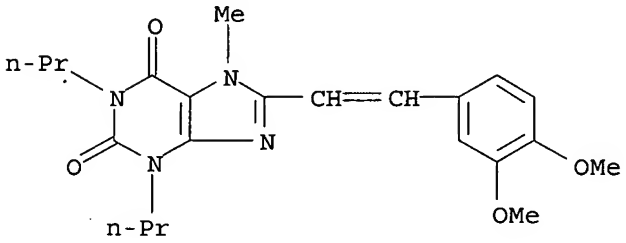
RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



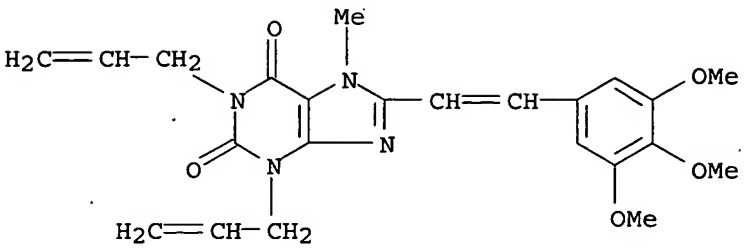
RN 31377-40-9 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 149744-74-1 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 193416-91-0 HCAPLUS
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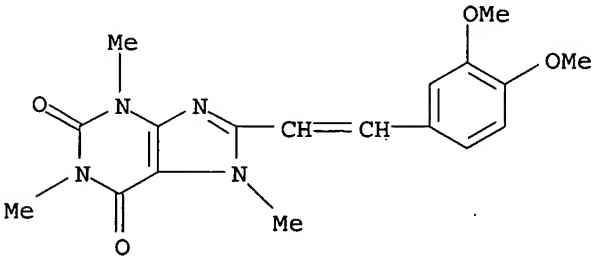

RN 193416-96-5 HCAPLUS
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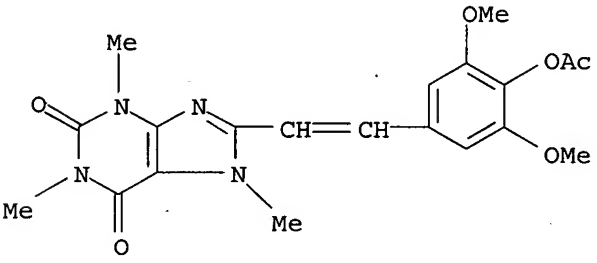
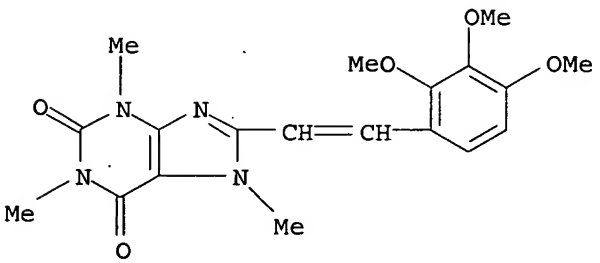
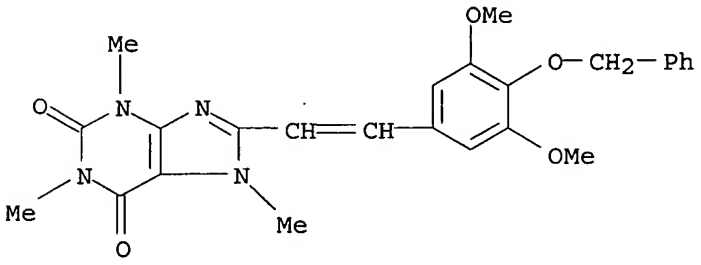


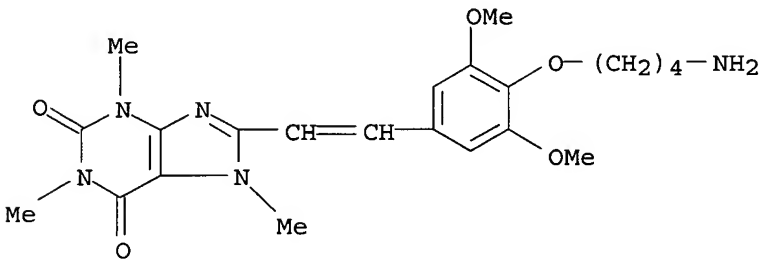
RN 193416-97-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



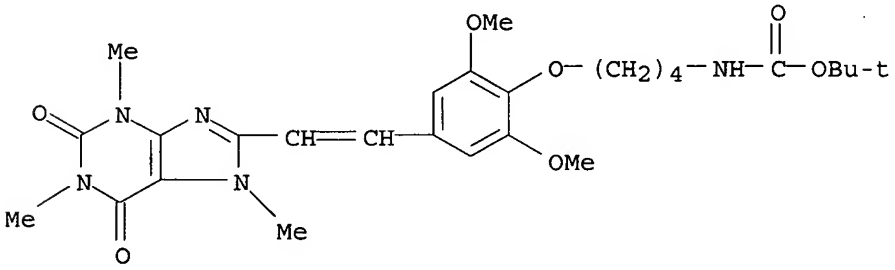
RN 212687-47-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 212687-48-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

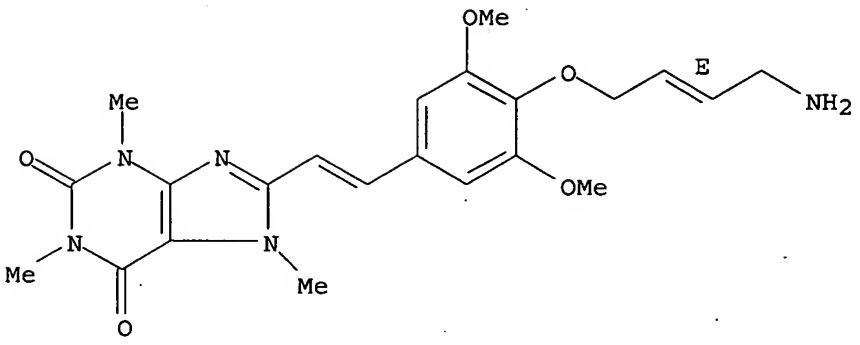


RN 212687-49-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



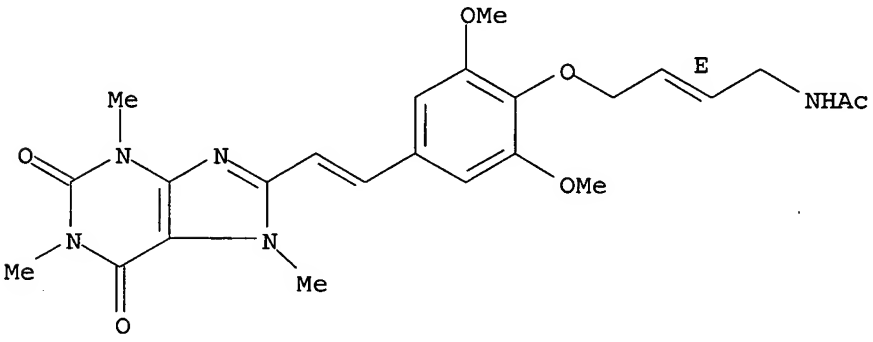
RN 212687-50-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



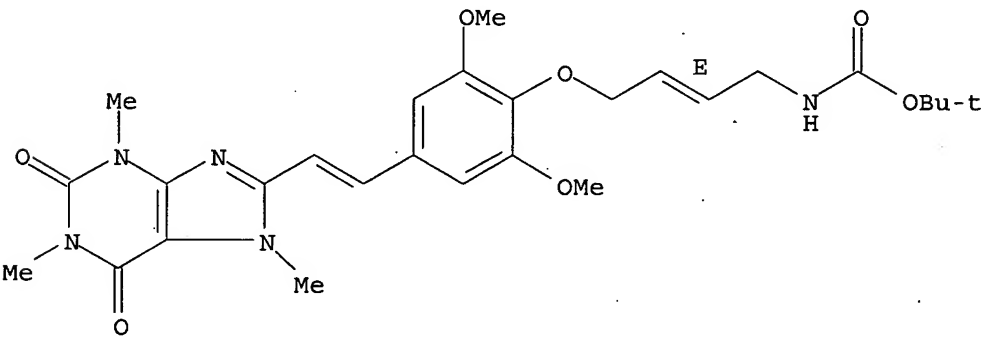
RN 212687-51-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



RN 212687-52-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



L34 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:978843 HCAPLUS

DOCUMENT NUMBER: 141:102286
TITLE: Potential of an adenosine A2A receptor antagonist [11C]TMSX for myocardial imaging by positron emission tomography: a first human study
AUTHOR(S): Ishiwata, Kiichi; Kawamura, Kazunori; Kimura, Yuichi; Oda, Keiichi; Ishii, Kenji
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Japan
SOURCE: Annals of Nuclear Medicine (2003), 17(6), 457-462
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous in vivo studies with mice, rats, cats and monkeys, we have demonstrated that [7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine ([11C]TMSX) is a potential radioligand for mapping adenosine A2A receptors of the **brain** by positron emission tomog. (PET). In the present study, we studied the potential of [11C]TMSX for myocardial imaging. Uptake of radioactivity by the heart was high and gradually decreased after an i.v. injection of [11C]TMSX into mice. In metabolite anal., 54% and 76% of the radioactivity in plasma and heart, resp., were present as the unchanged form of [11C]TMSX 60 min postinjection. The myocardial uptake was reduced by carrier-loading and by co-injection of an adenosine A2A antagonist CSC, but not by co-injection of an adenosine A1 antagonist DPCPX. Pretreatment with a high dose of a non-selective antagonist theophylline also reduced the myocardial uptake of [11C]TMSX. These findings demonstrate the specific binding of [11C]TMSX to adenosine A2A receptors in the heart. Finally we successfully performed the myocardial imaging by PET with [11C]TMSX in a normal volunteer. A graphical anal. by Logan plot supported the receptor-mediated uptake of [11C]TMSX. Peripherally [11C]TMSX was very stable in human: >90% of the radioactivity in plasma was detected as the unchanged form in a 60-min study. We concluded that [11C]TMSX PET has the potential for myocardial imaging.

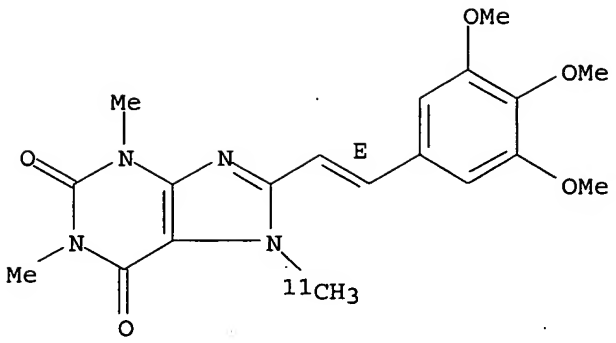
CC 8-9 (Radiation Biochemistry)

IT **223745-98-0**
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
(A2A receptor antagonist [11C]TMSX as PET agent for myocardial imaging)

IT **223745-98-0**
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
(A2A receptor antagonist [11C]TMSX as PET agent for myocardial imaging)

RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:677825 HCAPLUS
DOCUMENT NUMBER: 140:266862
TITLE: Preclinical studies on [11C]TMSX for mapping adenosine A2A receptors by positron emission tomography
AUTHOR(S): Ishiwata, Kiichi; Wang, Wei-Fang; Kimura, Yuichi; Kawamura, Kazunori; Ishii, Kenji
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Japan
SOURCE: Annals of Nuclear Medicine (2003), 17(3), 205-211
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous in vivo studies with mice, rats and monkeys, we have demonstrated that [11C]TMSX ([7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine) is a potential radioligand for mapping adenosine A2A receptors of the **brain** by positron emission tomog. (PET). In the present study, we performed a preclin. study. A suitable preparation method for [11C]TMSX injection was established. The radiation absorbed-dose by [11C]TMSX in humans estimated from the tissue distribution in mice was low enough for clin. use, and the acute toxicity and mutagenicity of TMSX were not found. The striatal uptake of [11C]TMSX in mice was reduced by pretreatment with theophylline at the dose of 10 and 100 mg/kg, suggesting that the [11C]TMSX PET should be carefully performed in the patients received with theophylline. We have concluded that [11C]TMSX is suitable for mapping adenosine A2A receptors in the human **brain** by PET.

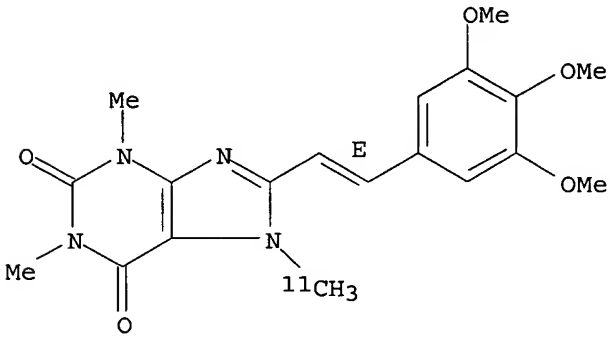
CC 8-9 (Radiation Biochemistry)
ST carbon 11 xanthine deriv adenosine receptor **brain** PET
IT **Brain**
Human
Positron-emission tomography
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)
IT **223745-98-0P**
RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); **PKT (Pharmacokinetics)**; PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)
IT **223745-98-0P**

RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); **PKT (Pharmacokinetics)**; PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
([11C]TMSX for mapping adenosine A2A receptors by positron emission tomog.)

RN 223745-98-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:904677 HCAPLUS

DOCUMENT NUMBER: 141:16533

TITLE: Translating A2A antagonist KW6002 from animal models to parkinsonian patients

AUTHOR(S): Chase, T. N.; Bibbiani, F.; Bara-Jimenez, W.; Dimitrova, T.; Oh-Lee, J. D.

CORPORATE SOURCE: National Institute of Neurological Disorders and Stroke, Experimental Therapeutics Branch, National Institutes of Health, Bethesda, MD, 20892-1406, USA

SOURCE: Neurology (2003), 61(11, Suppl. 6), S107-S111
CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Improving the translation of novel findings from basic laboratory research to better therapies for neurol. disease constitutes a major challenge for the neurosciences. This brief review of aspects of the development of an adenosine A2A antagonist for use in the management of Parkinson's disease (PD) illustrates approaches to some of the relevant issues. Adenosine A2A receptors, highly expressed on striatal medium spiny neurons, signal via kinases whose aberrant activation has been linked to the appearance of parkinsonian signs after dopaminergic denervation and to the motor response complications produced by dopaminomimetic therapy. To assess the ability of A2A receptor blockade to normalize certain of these kinases and thus benefit motor dysfunction, the palliative and prophylactic effects of the selective antagonist KW6002 were first evaluated in rodent and primate models. In hemiparkinsonian rats, KW6002 reversed the intermittent L-dopa treatment-induced, protein kinase A-mediated hyperphosphorylation of striatal α-amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid receptor GluR1 S845 residues and the

concomitant shortening in motor response duration. In 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned monkeys, coadministration of KW6002 with daily apomorphine injections acted prophylactically to prevent dyskinesia onset. These and related preclin. observations guided the design of a limited, randomized, controlled, proof-of-concept study of the A2A antagonist in patients with moderately advanced PD. Although KW6002 alone or in combination with a steady-state IV infusion of optimal-dose L-dopa had no effect on parkinsonian severity, the drug potentiated the antiparkinsonian response to low-dose L-dopa with fewer dyskinesias than produced by optimal-dose L-dopa alone. KW6002 also safely prolonged the efficacy half-time of L-dopa. The results suggest that drugs capable of selectively blocking adenosine A2A receptors could confer therapeutic benefit to L-dopa-treated parkinsonian patients and warrant further evaluation in phase II studies. They also illustrate a strategy for successfully bridging a novel approach to PD therapy from an evolving research concept to pivotal clin. trials.

CC 1-0 (Pharmacology)

IT **Brain**
(corpus striatum; translating A2A antagonist KW6002 from animal models to parkinsonian patients)

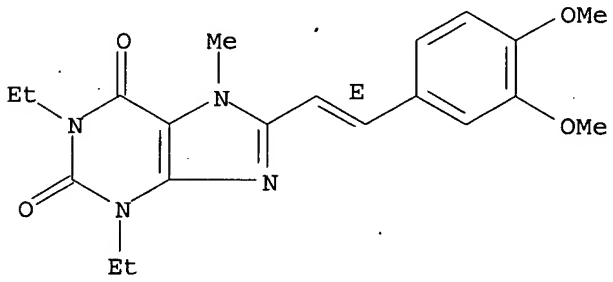
IT **155270-99-8**, KW6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(translating A2A antagonist KW6002 from animal models to parkinsonian patients)

IT **155270-99-8**, KW6002
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(translating A2A antagonist KW6002 from animal models to parkinsonian patients)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:793451 HCAPLUS
DOCUMENT NUMBER: 137:289033
TITLE: Adenosine A2A receptor antagonists combined with neurotrophic activity compounds in the treatment of Parkinson's disease

INVENTOR(S): Peters, Dan; Ronn, Lars Christian; Nielsen, Karin Sandager
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080957	A1	20021017	WO 2002-DK228	20020404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440196	AA	20021017	CA 2002-2440196	20020404
EP 1379269	A1	20040114	EP 2002-759761	20020404
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529916	T2	20040930	JP 2002-578996	20020404
US 2004097540	A1	20040520	US 2003-473809	20031002

PRIORITY APPLN. INFO.: DK 2001-583 A 20010409
WO 2002-DK228 W 20020404

AB This invention relates to the use of the combined action of a compound with neurotrophic activity and an adenosine A2A receptor antagonist for the treatment of Parkinson's disease. Adenosine A2A receptor antagonist is selected from the group consisting of KW-6002, ZM-241385, 8FB-PTP, SCH-58261, KF-17837, CGS-15943, DMPX, and pharmaceutically acceptable salts thereof. A compound with neurotrophic activity is selected from the group consisting of 5-(4-Chlorophenyl)-8-methyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]isoquinoline-2,3-dione-3-oxime; 5-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-h]naphthalene-2,3-dione-3-oxime; GDNF; Neublastin; and pharmaceutically acceptable salts thereof.

IC ICM A61K038-18
ICS A61K031-00; C07D473-04; C07K014-475; A61P025-16

CC 1-11 (Pharmacology)
Section cross-reference(s): 2

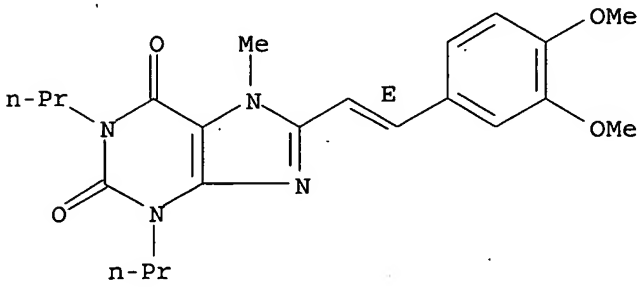
IT **Brain**
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT 14114-46-6, DMPX 104615-18-1, CGS-15943 139180-30-6, ZM-241385 **141807-96-7**, KF-17837 **155270-99-8**, KW-6002 160098-96-4, SCH-58261 160753-58-2 309711-72-6
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic compds. in treatment of Parkinson's disease)

IT **141807-96-7**, KF-17837 **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonists combined with neurotrophic compds.

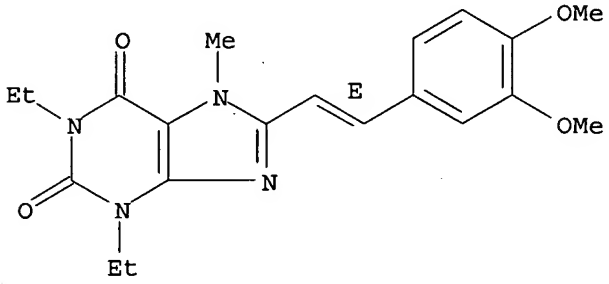
in treatment of Parkinson's disease)
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:90903 HCAPLUS
DOCUMENT NUMBER: 136:277364
TITLE: Neuroprotection by adenosine A2A receptor blockade in experimental models of Parkinson's disease
AUTHOR(S): Ikeda, Ken; Kurokawa, Masako; Aoyama, Shiro; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411-8731, Japan
SOURCE: Journal of Neurochemistry (2002), 80(2), 262-270
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the

present study, a significant neuroprotective effect of A2A receptor antagonists is shown in exptl. models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The neuroprotective property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically neuroprotective activities.

CC 14-10 (Mammalian Pathological Biochemistry)

IT **Brain**
(corpus striatum; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT **Brain**
(nigrostriatal dopaminergic tract; adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

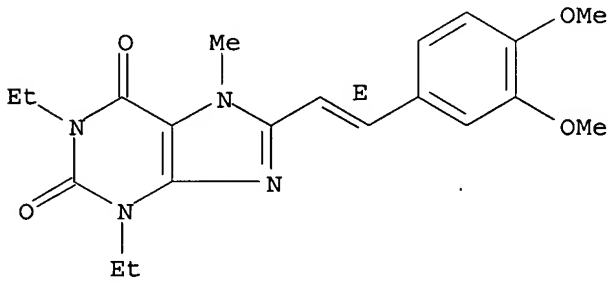
IT **155270-99-8**, KW-6002
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

IT **155270-99-8**, KW-6002
RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist neuroprotective property in exptl. models of Parkinson's disease)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 15 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002213683 EMBASE

TITLE: Adenosine as a neuroprotectant: Therapeutic perspectives.

AUTHOR: Phillis J.W.

CORPORATE SOURCE: Dr. J.W. Phillis, Department of Physiology, School of Medicine, Wayne State University, 540 E. Canfield Ave., Detroit, MI 48201, United States. jphillis@med.wayne.edu

SOURCE: Expert Review of Neurotherapeutics, (2002) Vol. 2, No. 2, pp. 167-176.
Refs: 81
ISSN: 1473-7175 CODEN: ERNXAR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020708
Last Updated on STN: 20020708

AB The potential for exploiting the neuroprotective properties of the purine nucleoside, adenosine, in a variety of CNS disorders, including: ischemic and traumatic injuries, neurodegenerative disorders, epilepsy and pain, has aroused considerable interest in both academic and pharmaceutical circles. A variety of approaches have been employed, ranging from the development of new selective agonists and antagonists for adenosine receptors, to compounds which can either potentiate extracellular levels of endogenously released adenosine or enhance its actions at receptors. Although many of these approaches were successful in animal studies, clinical trials have been delayed by the need to develop more potent and selective agents. With the recent promising advances in this area, future prospects for the development of new neurotherapeutic agents now appear promising.

CT Medical Descriptors:
*neuroprotection
brain ischemia
brain injury
degenerative disease
epilepsy
receptor intrinsic activity
human
review
Drug Descriptors:
*neuroprotective agent: DV, drug development
*neuroprotective agent: PD, pharmacology
*adenosine: DV, drug development
*adenosine: PD, pharmacology
purine nucleoside: DV, drug development
purine nucleoside: PD, pharmacology
adenosine receptor blocking agent: DV, drug development
adenosine receptor blocking agent: PD, pharmacology
adenosine receptor stimulating agent: DV, drug development
adenosine receptor stimulating agent: PD, pharmacology
adenosine A1 receptor agonist: DV, drug development
adenosine A1 receptor agonist: PD, pharmacology
adenosine A2a receptor agonist: DV, drug development
adenosine A2a receptor agonist: PD, pharmacology
adenosine A3 receptor agonist: DV, drug development
adenosine A3 receptor agonist: PD, pharmacology
adenosine A1 receptor antagonist: DV, drug development
adenosine A1 receptor antagonist: PD, pharmacology
adenosine A2 receptor antagonist: DV, drug development
adenosine A2 receptor antagonist: PD, pharmacology
adenosine A3 receptor antagonist: DV, drug development
adenosine A3 receptor antagonist: PD, pharmacology
cyclohexyladenosine: DV, drug development

cyclohexyladenosine: PD, pharmacology
6 n cyclopentyladenosine: DV, drug development
6 n cyclopentyladenosine: PD, pharmacology
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): DV, drug development
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): PD, pharmacology
6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine: DV, drug development
6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine: PD, pharmacology
8 cyclopentyltheophylline: DV, drug development
8 cyclopentyltheophylline: PD, pharmacology
8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine: DV, drug development
8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine: PD, pharmacology
4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol: DV, drug development
4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol: PD, pharmacology
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: DV, drug development
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: DV, drug development
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: PD, pharmacology
1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester: DV, drug development
1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester: PD, pharmacology
dipyridamole: DV, drug development
dipyridamole: PD, pharmacology
nitrobenzylthioinosine: DV, drug development
nitrobenzylthioinosine: PD, pharmacology
9 (2 hydroxy 3 nonyl)adenine: DV, drug development
9 (2 hydroxy 3 nonyl)adenine: PD, pharmacology
pentostatin: DV, drug development
pentostatin: PD, pharmacology
allopurinol: DV, drug development
allopurinol: PD, pharmacology
oxipurinol: DV, drug development
oxipurinol: PD, pharmacology
2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene: DV, drug development
2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene: PD, pharmacology
5 amino 4 imidazolecarboxamide riboside
unindexed drug

RN (adenosine) 58-61-7; (cyclohexyladenosine) 36396-99-3; (6 n cyclopentyladenosine) 41552-82-3; (2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide)) 120225-54-9; (6 n [2 (3,5 dimethoxyphenyl) 2 (2 methylphenyl)ethyl]adenosine) 120442-40-2; (8 cyclopentyltheophylline) 35873-49-5; (8 (2 amino 4 chlorophenyl) 1,3 dipropylxanthine) 85872-51-1; (4 [2 [7 amino 2 (2 furyl) 1,2,4 triazolo[2,3 a][1,3,5]triazin 5 ylamino]ethyl]phenol) 139180-30-6; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine) **155270-99-8**; (1,4 dihydro 2 methyl 6 phenyl 4 (2 phenylethynyl) 3,5 pyridinedicarboxylic acid 5 benzyl 3 ethyl ester) 185222-90-6; (dipyridamole) 58-32-2; (nitrobenzylthioinosine) 65177-80-2;

(9 (2 hydroxy 3 nonyl)adenine) 59262-86-1; (pentostatin) 53910-25-1; (allopurinol) 315-30-0; (oxipurinol) 2465-59-0; (2 amino 4,5 dimethyl 3 (3 trifluoromethylbenzoyl)thiophene) 132861-87-1; (5 amino 4 imidazolecarboxamide riboside) 2627-69-2

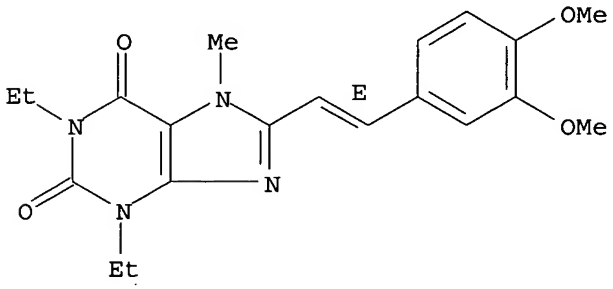
L34 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:787693 HCAPLUS
DOCUMENT NUMBER: 138:314421
TITLE: Distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in the rat **brain**
AUTHOR(S): Aoyama, Shiro; Koga, Kumiko; Mori, Akihisa; Miyaji, Hiromasa; Sekine, Susumu; Kase, Hiroshi; Uchimura, Tatsuo; Kobayashi, Hiroyuki; Kuwana, Yoshihisa
CORPORATE SOURCE: Pharmaceutical Res. Inst., Kyowa Hakko Kogyo Co. Ltd., Sunto-gun, Shizuoka, 411-8731, Japan
SOURCE: Brain Research (2002), 953(1,2), 119-125
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel adenosine A2A receptor selective antagonist, KW-6002 [(E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione], possesses antiparkinsonian activities in rodent and primate models. In the present study, the authors investigated the distribution of [14C]KW-6002 in forebrain after oral administration at pharmacol. EDs. Also, the authors monitored the effects of the compound on preproenkephalin (PPE) and preprotachykinin (PPT) gene expression in rat striatum. The highest level of radioactivity was observed in the striatum after oral administration of [14C]KW-6002; 30 min after 0.1 and 0.3 mg/kg, the d. values in the striatum were 2.45 and 2.43 times higher than those in a reference region (frontal cortex), resp. At the dose of 3 mg/kg, p.o., the ratio was only 1.58 and the compound was distributed more extensively in the **brain**. The distribution pattern and intensity of radioactivity were maintained even 90 min after the administration of [14C]KW-6002. Oral administration of KW-6002 (0.3 and 3 mg/kg/day) to rats for 14 days reversed the increased gene expression of PPE in striatum that had been depleted of dopamine by prior treatment with 6-hydroxydopamine (6-OHDA). On the other hand, KW-6002 did not alter the decreased gene expression of PPT in 6-OHDA-treated rats. These results are the 1st to show directly that orally administered KW-6002 is distributed selectively to the striatum and that it modulates the activity of striatopallidal enkephalin-containing neurons but not striatonigral substance P-containing neurons.

CC 1-11 (Pharmacology)
IT Adenosine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A2A, antagonist; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **Brain**
(corpus striatum; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT Antiparkinsonian agents
Parkinson's disease
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **Brain**
(forebrain; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)

IT Tachykinins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepro-; distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT 93443-35-7, Preproenkephalin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **PKT (Pharmacokinetics)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
IT **155270-99-8**, KW-6002
RL: **PAC (Pharmacological activity)**; **PKT (Pharmacokinetics)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(distribution of adenosine A2A receptor antagonist KW-6002 and its effect on gene expression in rat **brain**)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 17 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001430941 EMBASE
TITLE: Adenosine A(2A) receptor antagonists: Potential therapeutic neuroprotective effects in parkinson's disease.
AUTHOR: Morelli M.; Wardas J.
CORPORATE SOURCE: J. Wardas, Department of Neuropsychopharmacol., Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland. micmor@tin.it
SOURCE: Neurotoxicity Research, (2001) Vol. 3, No. 6, pp. 545-556.
Refs: 87
ISSN: 1029-8428 CODEN: NURRFI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020103
Last Updated on STN: 20020103

AB The most effective treatment of Parkinson's disease (PD) is, at present, the dopamine precursor L-3,4-dihydroxyphenyl-alanine (L-DOPA), however a number of disadvantages such as a loss of drug efficacy and severe side-effects (psychoses, dyskinesias and on-off phenomena) limit long-term, effective utilisation of this drug. Recent experimental studies in which selective antagonists of adenosine A(2A) receptors were used, have shown an improvement in motor disabilities in animal models of PD. The A(2A) antagonist [7-(2-phenylethyl)-5-amino-2-(2-furyl)-pyrazolo-(4,3-e)-1,2,4-triazolo(1,5--c)pyrimidine] (SCH 58261) potentiated the contralateral turning behavior induced by a threshold dose of L-DOPA or direct dopamine receptor agonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned rats, an effect accompanied by an increase in Foslike-immunoreactivity in neurons of the lesioned striatum. Likewise, other A(2A) receptor antagonists such as (3,7-dimethyl-1-propargylxanthine) (DMPX), [E-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine] (KF 17837) and [E-1,3-dietyl-8(3,4-dimethoxystyryl-7-methyl-3,7-dhydro-1H -purine-2,6-dione] (KW 6002) antagonized catalepsy induced by haloperidol or reserpine in the rat, whereas in non-human primate models of PD, KW 6002 reduced the rigidity and improved the disability score of MPTP-treated marmosets and cynomolgus monkeys. Moreover, in contrast to L-DOPA, selective A(2A) receptor antagonists administered chronically did not produce dyskinesias and did not evoke tolerance in 6-OHDA and MPTP models of PD. An additional therapeutic potential of adenosine A(2A) antagonists emerged from studies showing neuroprotective properties of these compounds in animal models of cerebral ischemia and excitotoxicity, as well as in the (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) (MPTP) model of PD. Adenosine A(2A) receptor antagonists by reversing motor impairments in animal models of PD and by contrasting cell degeneration are some of the most promising compounds for the treatment of PD.

CT Medical Descriptors:
*Parkinson disease: DT, drug therapy
drug activity
neuroprotection
drug efficacy
disease severity
psychosis: SI, side effect
dyskinesia: SI, side effect
long term care
drug utilization
motor dysfunction: DT, drug therapy
behavior
immunoreactivity
brain nerve cell
brain injury
corpus striatum
catalepsy: DT, drug therapy
primate
rigidity
disability
scoring system
marmoset
monkey
drug tolerance

brain ischemia: DT, drug therapy
brain ischemia: PC, prevention
neurotoxicity: DT, drug therapy
neurotoxicity: PC, prevention
nerve cell degeneration
human
nonhuman
mouse
rat
animal experiment
animal model
controlled study
article
priority journal
Drug Descriptors:
*5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
*adenosine receptor blocking agent: PD, pharmacology
levodopa: AE, adverse drug reaction
levodopa: DT, drug therapy
levodopa: PD, pharmacology
dopamine receptor stimulating agent
oxidopamine: PD, pharmacology
3,7 dimethyl 1 propargylxanthine: PD, pharmacology
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: DT, drug therapy
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: PD, pharmacology
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: DT, drug therapy
8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine: PD, pharmacology
haloperidol: TO, drug toxicity
reserpine: TO, drug toxicity
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: PK, pharmacokinetics
excitotoxin: TO, drug toxicity
bromocriptine
RN (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (levodopa) 59-92-7; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (3,7 dimethyl 1 propargylxanthine) 14114-46-6; (8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine) **141807-96-7** ; (8 (3,4 dimethoxystyryl) 1,3 diethyl 7 methylxanthine) **155270-99-8**; (haloperidol) 52-86-8; (reserpine) 50-55-5, 8001-95-4; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (bromocriptine) 25614-03-3

L34 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:811942 HCAPLUS
DOCUMENT NUMBER: 136:98481
TITLE: Evaluation of [4-O-methyl-11C]KW-6002 as a potential PET ligand for mapping central adenosine A2A receptors in rats
AUTHOR(S): Hirani, E.; Gillies, J.; Karasawa, A.; Shimada, J.; Kase, H.; Opacka-Juffry, J.; Osman, S.; Luthra, S. K.; Hume, S. P.; Brooks, D. J.
CORPORATE SOURCE: MRC Clinical Sciences Centre, Hammersmith Hospital, Imaging Research Solutions Ltd and PET Methodology Group, London, W12 0NN, UK
SOURCE: Synapse (New York, NY, United States) (2001), 42(3), 164-176
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB KW-6002, a xanthine-based adenosine A2A antagonist, was labeled with the positron emitter carbon-11 by O-methylation of its precursor, KF23325, using [11C]iodomethane and was evaluated in rats as a putative in vivo radioligand for positron emission tomog. (PET). Following i.v. injection of [11C]KW-6002, radioactivity was measured in blood, plasma, peripheral tissues, and in discrete **brain** tissues over a 2-h time period commensurate with PET scanning. In **brain**, [11C]KW-6002 showed highest retention in striata, with evidence of saturable binding, and lowest retention in frontal cortex (a tissue low in adenosine A2A receptors). PET scanning with [11C]KW-6002 demonstrated a specific signal in the striata which could be described using compartmental modeling. Specific binding was, however, also detected in extra-striatal regions, including **brain** areas reported to have low adenosine A2A receptor d. Blocking studies with the A1 selective antagonist KF15372 and the non xanthine-type A2A antagonist ZM 241385 failed to elucidate the nature of this binding. Thus, although [11C]KW-6002 shows some potential for development as a PET ligand for quantifying striatal adenosine A2A receptor function, its in vivo selectivity requires further investigation.

CC 8-9 (Radiation Biochemistry)

IT **Brain**
(corpus striatum, ligand distribution; [4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

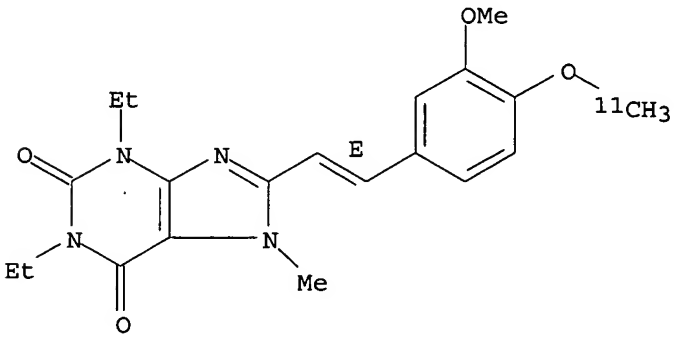
IT **389571-64-6**, [4-O-Methyl-11C]KW 6002
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
([4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

IT **389571-64-6**, [4-O-Methyl-11C]KW 6002
RL: DGN (Diagnostic use); **PKT (Pharmacokinetics)**; BIOL (Biological study); USES (Uses)
([4-O-methyl-11C]KW-6002 evaluation as potential PET ligand for mapping central adenosine A2A receptors)

RN 389571-64-6 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[(1E)-2-[3-methoxy-4-(methoxy-11C)phenyl]ethenyl]-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:135452 HCAPLUS

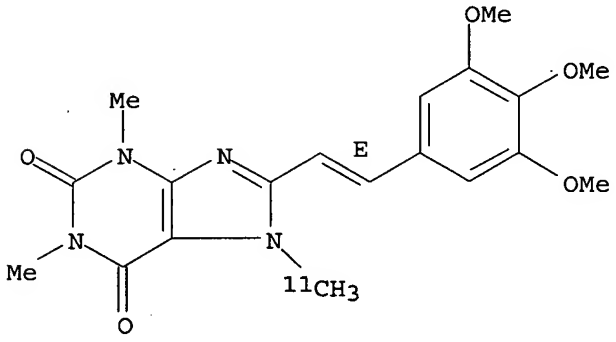
DOCUMENT NUMBER: 133:55385
TITLE: 11C-labeled KF18446: a potential central nervous system adenosine A2a receptor ligand
AUTHOR(S): Ishiwata, Kiichi; Noguchi, Junko; Wakabayashi, Shin-Ichi; Shimada, Junichi; Ogi, Nobuo; Nariai, Tadashi; Tanaka, Akira; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173-0022, Japan
SOURCE: Journal of Nuclear Medicine (2000), 41(2), 345-354
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To develop PET ligands for mapping central nervous system (CNS) adenosine A2a receptors that are localized in the striatum and are coupled with dopamine receptors, 3 11C-labeled xanthine-type adenosine A2a antagonists, [11C]KF18446 ([7-methyl-11C]-(E) -8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine), [11C]KF19631 ([7-methyl-11C]- (E)-1,3-diallyl-7-methyl-8- (3,4,5- trimethoxystyryl-)xanthine), and [11C]CSC ([7-methyl-11C] -8-chlorostyrylcaffeine), were compared with [11C]KF17837 ([7-methyl-11C]-(E)-8-(3,4-dimethoxystyryl) -1,3-dipropyl-7- methylxanthine). The regional **brain** uptake of the tracers, the effect of the coinjected adenosine antagonists on the uptake, and the metabolism were studied in mice. In rats, the regional **brain** uptake of the tracers was visualized by ex vivo autoradiog. (ARG). The A2a receptor binding of antagonist 1 was also measured by in vitro ARG. Imaging of the monkey **brain** was performed with PET with antagonist 1. In mice, the highest striatal uptake was found for antagonist 1 followed by antagonists 2 and 4. The uptake was inhibited by each of 3 KF compds. and by CSC, but not by an A1 antagonist KF15372. Another selective nonxanthine-type A2a antagonist SCH 58261 significantly decreased the striatal uptake of only antagonist 1, the labeled metabolites of which were less than 20% in the plasma 30 min postinjection, but were negligible in the **brain** tissue. In ex vivo ARG, antagonist 1 showed the highest striatal uptake and the highest uptake ratio of the striatum to the other **brain** regions. A high and selective binding of antagonist 1 to the striatum was also confirmed by in vitro ARG. PET with antagonist 1 visualized adenosine A2a receptors in the monkey striatum. These results indicate that antagonist 1 ([11C]KF18446) is the most suitable PET ligand for mapping adenosine A2a receptors in the CNS.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine A2a receptor carbon 11 KF18446
IT **Brain**
Positron-emission tomography
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
IT **223745-98-0**, [11C]KF 18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
IT **179678-39-8**, [11C]KF 17837 **278168-67-5**, [11C]KF 19631
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand: comparison with [11C]KF19631 and [11C]KF17837)

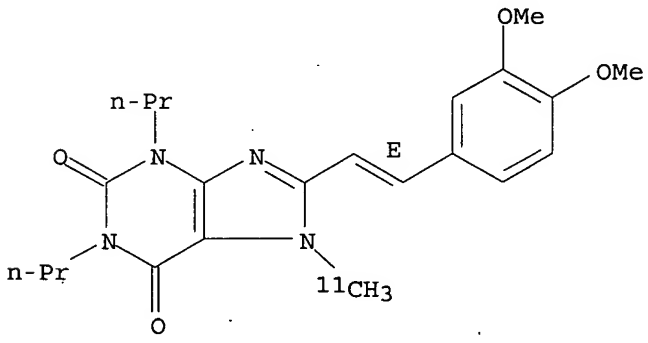
IT **223745-98-0**, [11C]KF 18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand)
RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



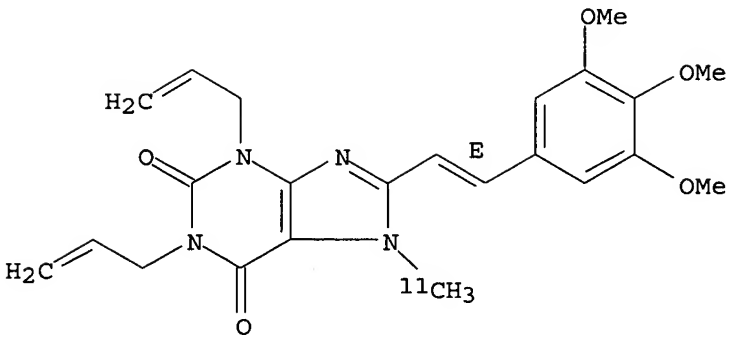
IT **179678-39-8**, [11C]KF 17837 **278168-67-5**, [11C]KF 19631
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(11C-labeled KF18446 as potential central nervous system adenosine A2a receptor ligand: comparison with [11C]KF19631 and [11C]KF17837)
RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 278168-67-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-(methyl-11C)-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:480897 HCAPLUS
DOCUMENT NUMBER: 133:346544
TITLE: Further characterization of a CNS adenosine A2a receptor ligand [11C]KF18446 with in vitro autoradiography and in vivo tissue uptake
AUTHOR(S): Ishiwata, Kiichi; Ogi, Nobuo; Shimada, Junichi; Nonaka, Hiromi; Tanaka, Akira; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173-0022, Japan
SOURCE: Annals of Nuclear Medicine (2000), 14(2), 81-89
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PET assessment of the adenosine A2a receptors localized in the striatum offers us a potential new diagnostic tool for neurol. disorders. In the present study, we carried out in vitro receptor autoradiog. of a newly developed PET ligand [11C]KF18446 ([7-methyl-11C]-(E)-8-(3,4,5-trimethoxystyryl)-1,3,7-trimethylxanthine) with rat **brain** sections. [11C]KF18446 showed a high striatum/cortex binding ratio (5.0) and low nonspecific binding (<10%), suggesting that [11C]KF18446 has characteristics comparable or slightly superior to [3H]CGS 21680 or [3H]SCH 58261, which are currently available representative A2a receptor ligands. Scatchard anal. indicated a Kd of 9.8 nM and a Bmax of 170 fmol/mm3 tissue in the striatum and a Kd of 16.4 nM and a Bmax of 33 fmol/mm3 tissue in the cortex. Seven xanthine-type and four nonxanthine-type adenosine receptor ligands with an affinity for the adenosine A2a receptors significantly reduced the in vitro binding of [11C]KF18446 to the **brain** section. The blocking effects were much stronger in the striatum than in the cortex, but did not necessarily parallel their affinity. On the other hand, four xanthine-type ligands and one nonxanthine-type ligand (SCH.58261) of the 11 ligands studied reduced the in vivo uptake of [11C]KF18446 in mice, but other ligands, including A1-selective and nonselective ligands and three nonxanthine-type A2a-selective antagonists did not. We conclude that [11C]KF18446 is a promising adenosine A2a receptor ligand for PET study.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine receptor autoradiog carbon 11 KF18446
IT **Brain**
Positron-emission tomography

(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

IT **223745-98-0**, [11C]KF18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

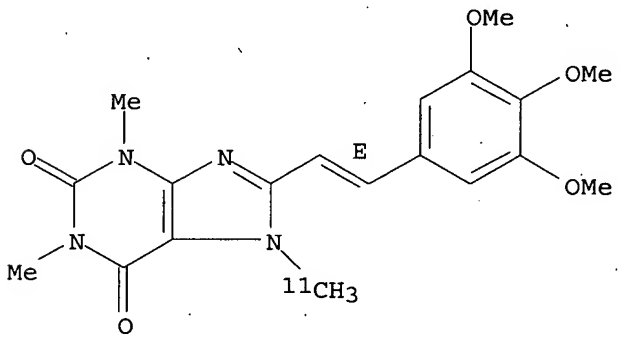
IT 120225-54-9, CGS 21680
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine agonist)

IT 14114-46-6, 3,7-Dimethyl-1-propargylxanthine **51389-37-8**, KF 18446 91896-57-0, CP 66713 96865-92-8, XAC 131080-42-7, KF 15372 139180-30-6, ZM 241385 **141807-96-7**, KF 17837 **142665-36-9**, KF 19631 147700-11-6, 8-(3-Chlorostyryl)caffeine 158747-27-4, ZD 9255 160098-96-4, SCH 58261
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine antagonists)

IT **223745-98-0**, [11C]KF18446
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(CNS adenosine A2a receptor ligand [11C]KF18446: autoradiog. and tissue uptake)

RN 223745-98-0 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

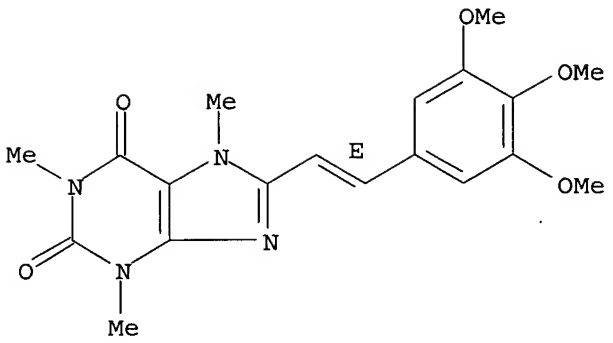
Double bond geometry as shown.



IT **51389-37-8**, KF 18446 **141807-96-7**, KF 17837 **142665-36-9**, KF 19631
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(CNS adenosine A2a receptor ligand [11C]KF18446: blockade of binding in **brain** by adenosine antagonists)

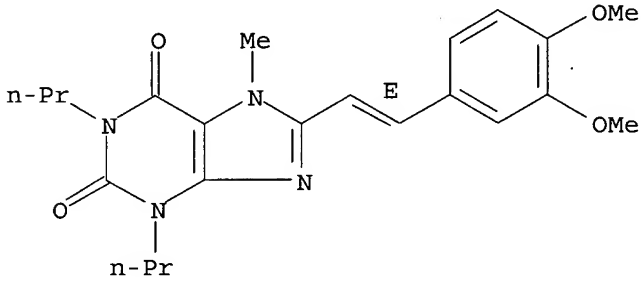
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



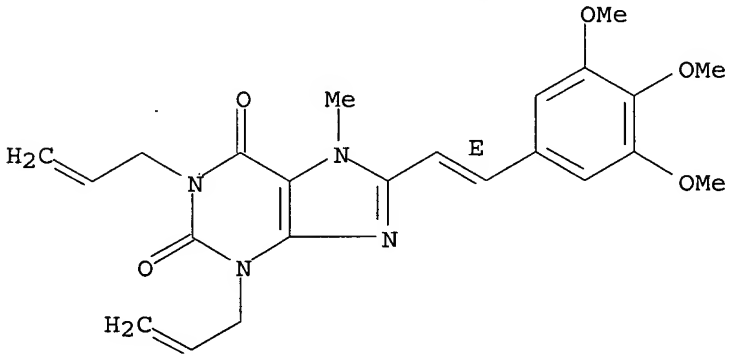
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:637359 HCAPLUS

DOCUMENT NUMBER: 134:430
TITLE: Systemic administration of adenosine A2A receptor antagonist reverses increased GABA release in the globus pallidus of unilateral 6-hydroxydopamine-lesioned rats: a microdialysis study
AUTHOR(S): Ochi, M.; Koga, K.; Kurokawa, M.; Kase, H.; Nakamura, J.; Kuwana, Y.
CORPORATE SOURCE: Kyowa Hakko Kogyo, Pharmaceutical Research Institute, Nagaizumi, Sunto, Shizuoka, 411-8731, Japan
SOURCE: Neuroscience (Oxford) (2000), 100(1), 53-62
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of adenosine A2A receptor antagonists to exhibit antiparkinsonian activity has recently been reported, but the mechanisms of action are still unknown. Since A2A receptors have been localized to GABAergic striatopallidal neurons, it is probable that these antagonists affect the activity of these neurons. In the present study, extracellular GABA basal levels were increased in the ipsilateral striatum and globus pallidus following a unilateral 6-hydroxydopamine lesion of the nigrostriatal pathway. The A2A receptor-selective antagonist KW-6002 (3 mg/kg, p.o.) caused a marked and sustained decrease of extracellular GABA levels in the globus pallidus of the 6-hydroxydopamine-lesioned rats, whereas no changes in GABA levels were observed in the globus pallidus of the non-lesioned rats. Microinjection of the A2A receptor agonist CGS21680 (0.005-0.5 μg) into the striatum of non-lesioned animals increased GABA concns. in the globus pallidus, which was abolished by the voltage-dependent Na+ channel blocker tetrodotoxin (1 μmol/l) delivered locally to the globus pallidus via the dialysis membrane. Furthermore, intrapallidal infusion of CGS21680 (10 μmol/l) also increased GABA levels in the globus pallidus. These data indicate that GABA release from striatopallidal neurons is regulated through A2A receptors in both the striatum and globus pallidus. The reversal of the 6-hydroxydopamine-induced increase in pallidal GABA levels by KW-6002 suggests that the antiparkinsonian effects of A2A receptor antagonists occur on the striatopallidal neurons.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 13, 14

IT **Brain**
(corpus striatum, GABAergic system; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **Brain**
(globus pallidus; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

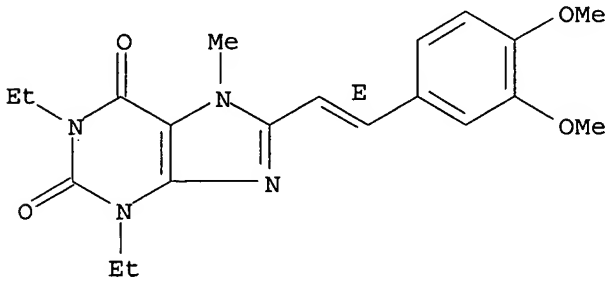
IT **Brain**
(striatopallidonigral tract; adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **155270-99-8**, KW-6002
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)

IT **155270-99-8**, KW-6002
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptor antagonist reverses increased GABA release in globus pallidus of unilateral 6-hydroxydopamine-lesioned rats)
RN 155270-99-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:282105 HCAPLUS
DOCUMENT NUMBER: 130:306595
TITLE: Methods for reducing ischemic injury of the heart via the sequential administration of synergistic cardioprotective agents
INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA; National Institute of Health
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9920284	A1	19990429	WO 1998-US22515		19981023
W: AU, CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9913636	A1	19990510	AU 1999-13636		19981023
US 6329349	B1	20011211	US 2000-530164		20000424
PRIORITY APPLN. INFO.:			US 1997-62737P	P	19971023
			WO 1998-US22515	W	19981023

AB Materials and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment comprises methods of sequential administration of a plurality of cardioprotective agents (e.g. monophosphoryl lipid A and adenosine receptor agents).
IC ICM A61K031-715
ICS A61K031-44
CC 1-8 (Pharmacology)
Section cross-reference(s): 63

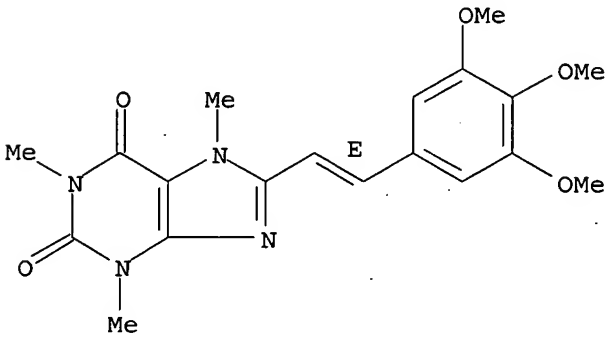
IT **Anti-ischemic agents**
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

IT 58-61-7, Adenosine, biological studies 16561-29-8, Phorbol 12-myristate 13-acetate 37739-05-2, 2-Chloro-N6-cyclopentyladenosine **51389-37-8** 60560-33-0, Pinacidil 65141-46-0, Nicorandil 96760-69-9 99765-13-6 103201-24-7 **141807-96-7** **142665-36-9** 147699-95-4 147699-98-7 147700-00-3 147700-02-5 147700-04-7 147700-05-8 147700-06-9 147700-07-0 147700-08-1 147700-10-5 147700-11-6 147700-13-8 **147700-19-4** 147700-20-7 147700-21-8 147700-23-0 147700-24-1 **147700-25-2** **147700-26-3** **147700-27-4** **147700-28-5** **147700-29-6** **147700-30-9** **147700-31-0** **147700-33-2** **147700-40-1** 147700-46-7 151539-31-0 152918-18-8 152918-28-0, MRS 1340 152918-39-3 163042-87-3, MRS 584 163152-33-8, MRS 537 163259-37-8, MRS 479 170966-25-3 173845-91-5 173846-04-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

IT **51389-37-8** **141807-96-7** **142665-36-9** **147700-19-4** **147700-25-2** **147700-26-3** **147700-27-4** **147700-28-5** **147700-29-6** **147700-30-9** **147700-31-0** **147700-33-2** **147700-40-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(heart ischemic injury reduction by sequential administration of synergistic cardioprotective agents)

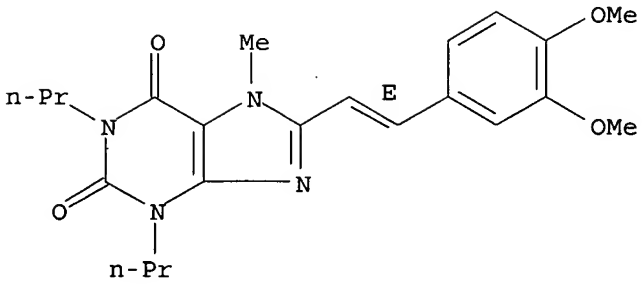
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



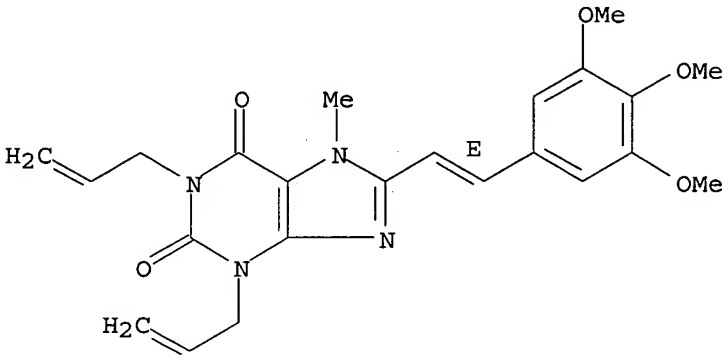
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



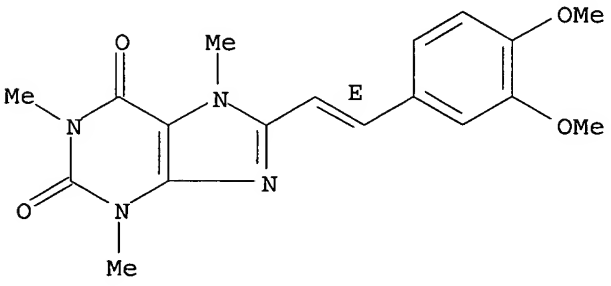
RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



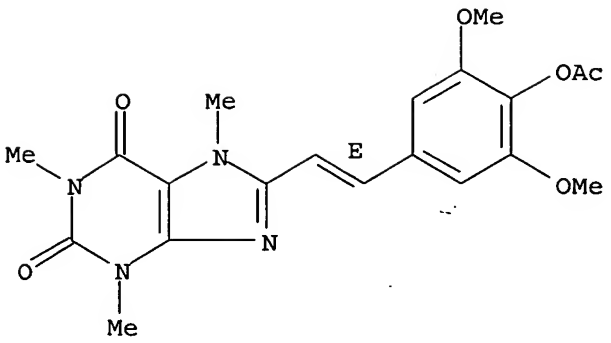
RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



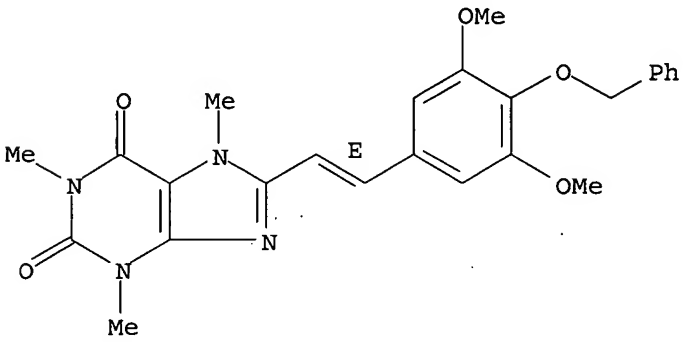
RN 147700-25-2 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



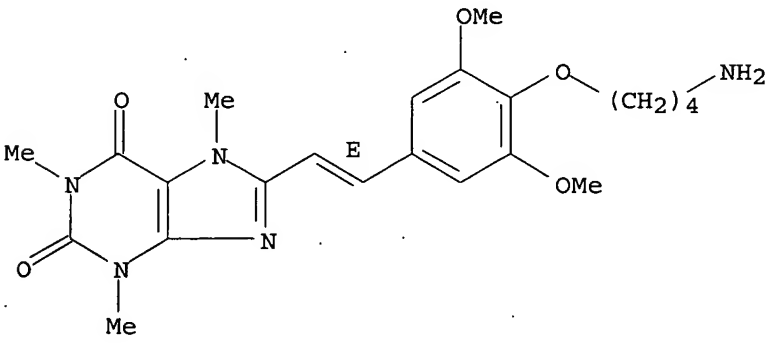
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

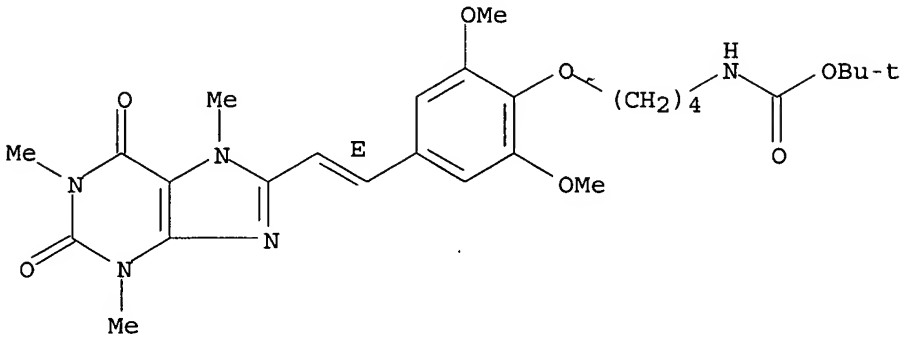
Double bond geometry as shown.



RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-,

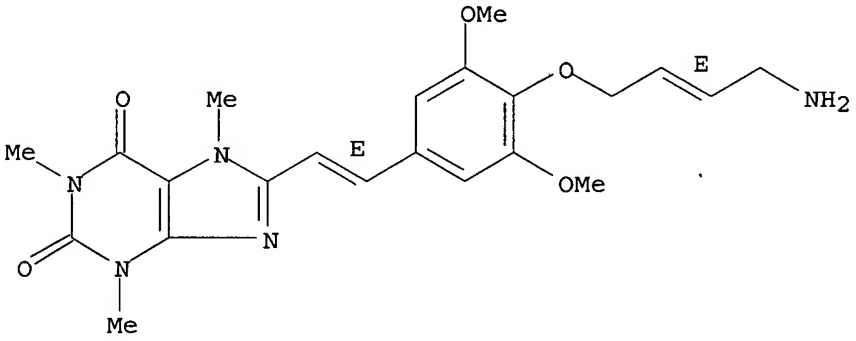
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



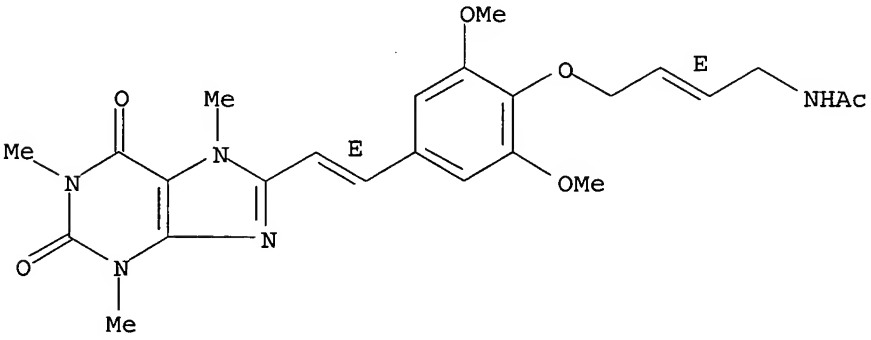
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



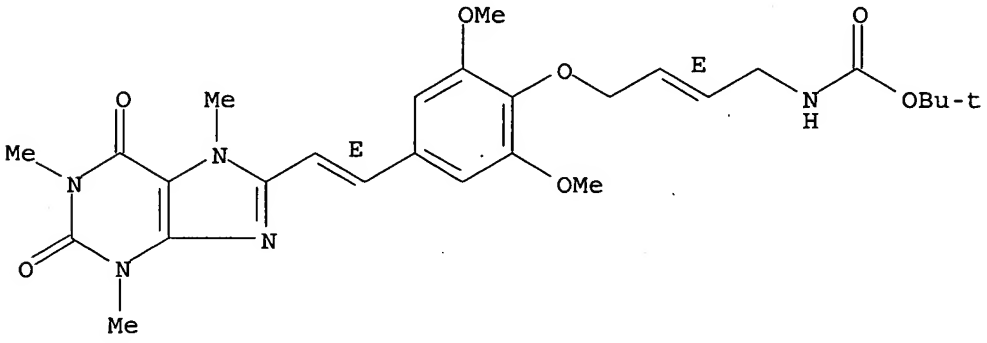
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



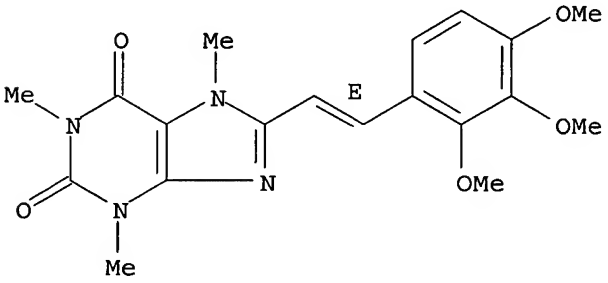
RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



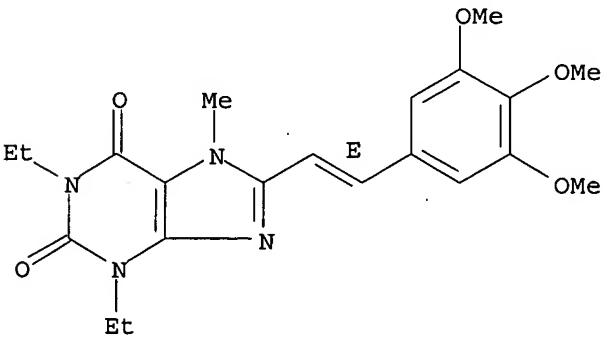
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

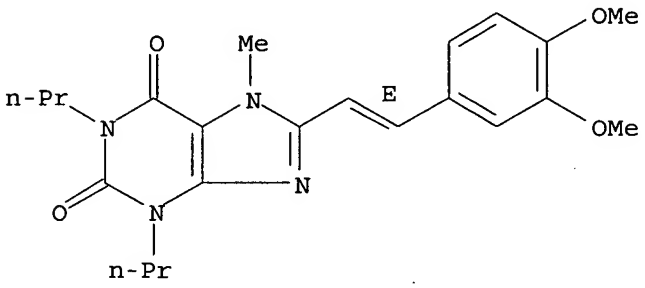
L34 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:693087 HCAPLUS
DOCUMENT NUMBER: 132:347
TITLE: Autoradiographic comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors
AUTHOR(S): Fredholm, Bertil B.; Lindstrom, Karin
CORPORATE SOURCE: Department of Physiology and Pharmacology, Section of Molecular Neuropharmacology, Karolinska Institutet, Stockholm, S-171 77, Swed.
SOURCE: European Journal of Pharmacology (1999), 380(2/3), 197-202
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have examined the potency of several adenosine receptor antagonists at adenosine A1 and A2A receptors using quant. autoradiog. and have compared the results with those of previous studies using the same radioligands in membrane prepns. The agonists [3H]cyclohexyladenosine and [3H]2-[p-(2-carbonylethyl)-phenylethylamino]-5'-N-ethylcarboxamido adenosine ([3H]CGS 21680) were used as radioligands for the two receptors. The results show that 1,3-dipropyl-8-cyclopentyl xanthine (DPCPX) is almost 1000-fold and 8-chloro-4-cyclohexyl-amino-1-(trifluoromethyl)[1,2,4]triazolo[4,3-a]quinoxaline (CP-68,247) about 300-fold more potent at adenosine A1 receptors in cortex and striatum than at striatal adenosine A2A receptors. Conversely, 5-amino-7-(2-phenylethyl)-2-(2-furyl)-pyrazolo-[4,3-e]-1,2,4-triazolo [1,5-c]pyrimidine (SCH 58261) is approx. 1000-fold and 4-(2-[7-amino-2-(2-furyl)[1,2,4]-triazolo[2,3-a][1,3,5]triazin-5-yl amino]ethyl)phenol (ZM 241,385) about 400-fold more potent at adenosine A2A than at A1 receptors. Caffeine and its metabolites did not show any selectivity. Other studied antagonists were non-selective or showed a modest (20- to 40-fold) adenosine A2A receptor selectivity. Thus, only a few of the antagonists show such high selectivity that it is not offset by differences in drug distribution and levels of receptor subtype expression.

CC 1-11 (Pharmacology)
ST autoradiog adenosine receptor antagonist **brain**
IT **Brain**
(cerebral cortex; autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
IT **Brain**
(corpus striatum; autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 83-67-0, Theobromine 611-59-6, Paraxanthine 91895-50-0 91896-57-0, CP-66713 102146-07-6, 1,3-Dipropyl-8-cyclopentyl xanthine 104615-18-1, CGS 15943 127710-75-2, CP-68247 139180-30-6, ZM 241385 **141807-96-7**, KF 17837 147700-11-6 160098-96-4, SCH 58261
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A

receptors)
IT **141807-96-7**, KF 17837
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autoradiog. comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A1 and A2A receptors)
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:334755 HCAPLUS
DOCUMENT NUMBER: 131:111326
TITLE: Effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice
AUTHOR(S): De Sarro, Giovambattista; De Sarro, Angela; Di Paola, Eugenio Donato; Bertorelli, Rosalia
CORPORATE SOURCE: Department of Experimental and Clinical Medicine, School of Medicine, University of Catanzaro, Catanzaro, 88100, Italy
SOURCE: European Journal of Pharmacology (1999), 371(2/3), 137-145
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have studied the effects of selective and non-selective adenosine receptor agonists and antagonists in audiogenic-seizure-sensitive DBA/2 mice, an animal model of generalized reflex epilepsy. With the exception of the adenosine A3 receptor agonist, N6-(3-iodobenzyl)-5'-N-methylcarboxamidoadenosine (IB-MECA), all the agonists studied prevented the development of audiogenic seizures in a dose-dependent manner. The ED50 values against the clonic phase of the audiogenic seizures were low, that is: 0.06 mg/kg, i.p., for the adenosine A1 receptor agonist, 2-chloro-N6-cyclopentyladenosine (CCPA), 0.02 and 0.03 mg/kg, i.p., for the adenosine A2A receptor agonists, 2-(4-(2-carboxyethyl)-phenylamino)-5'-N-ethylcarboxamidoadenosine (CGS 21680) and 2-hexynyl-5'-N-ethyl-carboxamidoadenosine (2-HE-NECA), and 0.7 mg/kg, i.p., for the adenosine Aj/A3 receptor agonist, N6-2-(4-aminophenyl)ethyladenosine (APNEA). Conversely, the non-selective agonist, N-ethyl-carboxamidoadenosine

(NECA), was highly potent, the ED50 being 0.0005 mg/kg, i.p. In the absence of auditory stimulation, the adenosine receptor antagonists increased the incidence of both clonic and tonic seizures in DBA/2 mice. The ED50 values were: for caffeine, 207.5 mg/kg, i.p., for the adenosine A, receptor antagonist, 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), 327.8 mg/kg i.p., for the adenosine A2A receptor antagonists, 3,7-dimethyl-1-propylxanthine (DPMX), 86.7 mg/kg i.p., for the (E,18%-Z,82%)7-methyl-8-(3,4-dimethoxystyryl)-1,3-dipropylxanthine (KF 17837), 69.1 mg/kg i.p., and 5-amino-7-(2-phenylethyl)-2-(2-furyl)-pyrazolo-(4,3-c)1,2,4-triazolo(1,5-c)-pyrimidine (SCH 58261), 321.8 mg/kg i.p. The rank order of convulsant potency in our epileptic model, following intracerebroventricular administration, was DPCPX > DMPX > 1,3,7-trimethyl-8-(3-chlorostyryl)xanthine (CSC) > KF 17837 > Caffeine > SCH 58261 > 5-amino-9-chloro-2-(2-furyl)-1,2,4-triazolo(1,5-c)quinazoline (CGS 15943). Following a subconvulsant audiogenic stimulus of 83 dB, all adenosine receptor antagonists induced both tonic and clonic seizures. The ED50 values for such proconvulsant effects were: for caffeine 0.04 mg/kg, i.p., for the adenosine A, receptor antagonist, DPCPX, 5.84 mg/kg, i.p., for the adenosine A2A receptor antagonists, DMPX, 0.02 mg/kg, i.p., CGS 15943, 0.29 mg/kg i.p., KF 17837, 0.57 mg/kg, i.p., CSC 0.12 mg/kg, i.p. and SCH 58261 0.07 mg/kg, i.p., resp. These data suggest that stimulation of adenosine A1 and A2A receptors is involved in the suppression of seizures.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 14

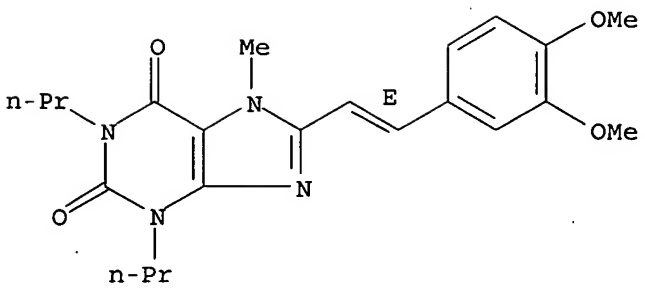
IT Anticonvulsants
Blood-**brain** barrier
Disease models
Epilepsy
Neurotransmission
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

IT 63906-63-8, 3,7-Dimethyl-1-propylxanthine 102146-07-6, DPCPX
141807-96-7, KF 17837 148589-13-3 160098-96-4, SCH 58261
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

IT **141807-96-7**, KF 17837
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice)

RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

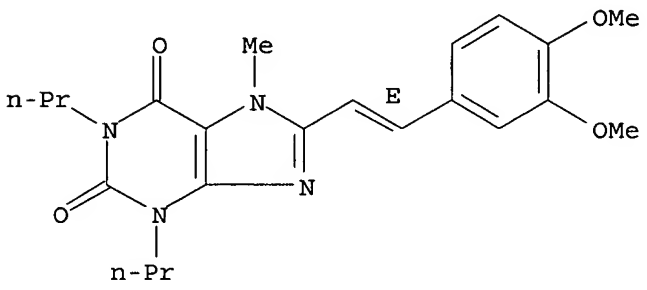


REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:713015 HCAPLUS
DOCUMENT NUMBER: 132:161113
TITLE: Effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice. [Erratum to document cited in CA131:111326]
AUTHOR(S): De Sarro, Giobambattista; De Sarro, Angela; Di Paola, Eugenio Donato; Bertorelli, Rosalia
CORPORATE SOURCE: Dep. Exp. and Clinical Med., Sch. Med., Univ. Catanzaro, Catanzaro, 88100, Italy
SOURCE: European Journal of Pharmacology (1999), 382(1), 51
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Table 3 has an error concerning the CD50 value of caffeine; the exact value is 192.8 (161.6-230.1).
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 14
ST erratum adenosine receptor agonist anticonvulsant epilepsy; adenosine receptor agonist anticonvulsant epilepsy erratum; receptor agonist anticonvulsant epilepsy model erratum; proconvulsant adenosine receptor antagonist epilepsy erratum; pharmacokinetic interaction anticonvulsant adenosine agonist erratum; blood **brain** barrier anticonvulsant adenosine agonist erratum; barrier anticonvulsant adenosine agonist epilepsy erratum
IT Anticonvulsants
Blood-**brain** barrier
Disease models
Epilepsy
Neurotransmission
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
IT 63906-63-8, 3,7-Dimethyl-1-propylxanthine 102146-07-6, DPCPX **141807-96-7**, KF 17837 148589-13-3 160098-96-4, SCH 58261
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
IT **141807-96-7**, KF 17837
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)

(effects of adenosine receptor agonists and antagonists on audiogenic seizure-sensible DBA/2 mice (Erratum))
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



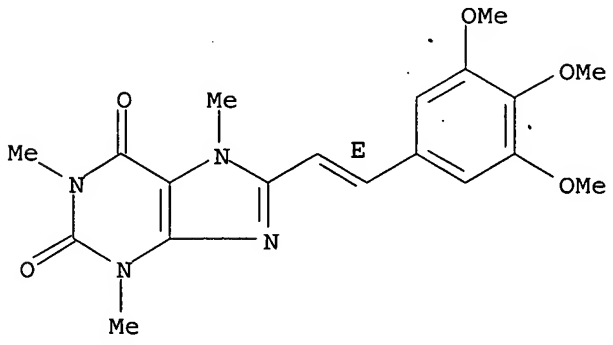
L34 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:744957 HCAPLUS
DOCUMENT NUMBER: 130:10632
TITLE: Methods and compositions for reducing ischemic injury of the heart by administering adenosine receptor agonists and antagonists
INVENTOR(S): Liang, Bruce T.; Jacobson, Kenneth A.
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850047	A1	19981112	WO 1998-US9031	19980508
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2289731	AA	19981112	CA 1998-2289731	19980508
AU 9873677	A1	19981127	AU 1998-73677	19980508
AU 750322	B2	20020718		
EP 991414	A1	20000412	EP 1998-920958	19980508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6211165	B1	20010403	US 1999-423129	19991105
PRIORITY APPLN. INFO.:			US 1997-46030P P	19970509
			US 1997-61716P P	19971010
			WO 1998-US9031 W	19980508

AB Compns. and methods for reducing or preventing ischemic damage of the heart are disclosed. A preferred embodiment of the invention comprises the simultaneous administration of specific A3/A1 receptor agonists, to patients suffering from ischemic damage or at risk for the same. In yet another embodiment of the invention, a binary conjugate which acts as an agonist for the A3 receptor and an antagonist at the A2a receptor, is administered to reduce or prevent ischemic damage to the heart.

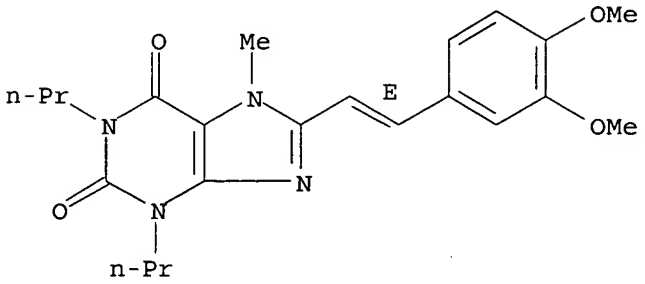
IC ICM A61K031-70
CC 1-8 (Pharmacology)
Section cross-reference(s): 33
IT **Anti-ischemic agents**
Protein sequences
Purinoceptor agonists
Purinoceptor antagonists
cDNA sequences
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
IT 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine 41552-82-3
51389-37-8 99765-13-6 103201-24-7 139180-30-6, ZM241385
141807-96-7 142665-36-9 147699-95-4 147699-98-7
147700-00-3 147700-02-5 147700-04-7 147700-05-8 147700-06-9
147700-07-0 147700-08-1 147700-10-5 147700-11-6 147700-13-8
147700-19-4 147700-20-7 147700-21-8 147700-23-0
147700-24-1 **147700-25-2 147700-26-3**
147700-27-4 147700-28-5 147700-29-6
147700-30-9 147700-31-0 147700-33-2
147700-40-1 147700-46-7 151539-31-0 152918-28-0
152918-39-3 160098-96-4, SCH58261 162684-35-7 163042-87-3
163152-33-8 163259-37-8 169190-74-3 170966-25-3 173845-91-5
173846-04-3 196497-15-1 199680-67-6 215933-83-8 215933-84-9
215933-88-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
IT **51389-37-8 141807-96-7 142665-36-9**
147700-19-4 147700-25-2 147700-26-3
147700-27-4 147700-28-5 147700-29-6
147700-30-9 147700-31-0 147700-33-2
147700-40-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. for reducing ischemic injury of heart by administering adenosine receptor agonists and antagonists)
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



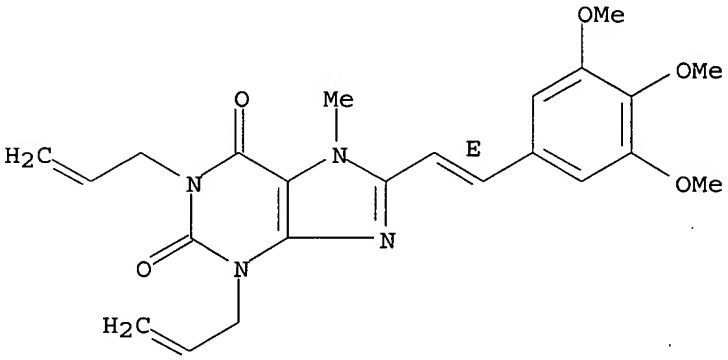
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



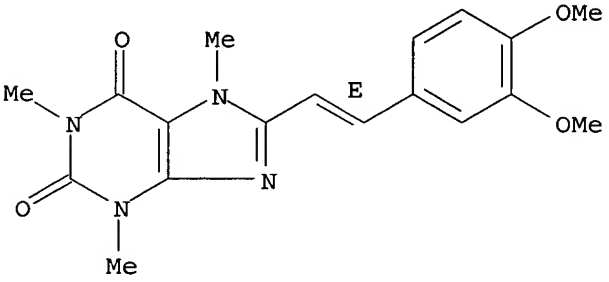
RN 142665-36-9 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

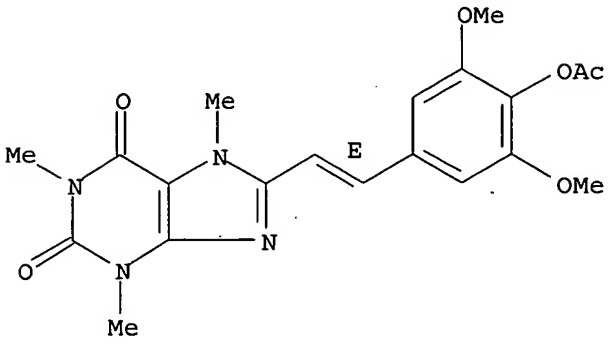
Double bond geometry as shown.



RN 147700-25-2 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-

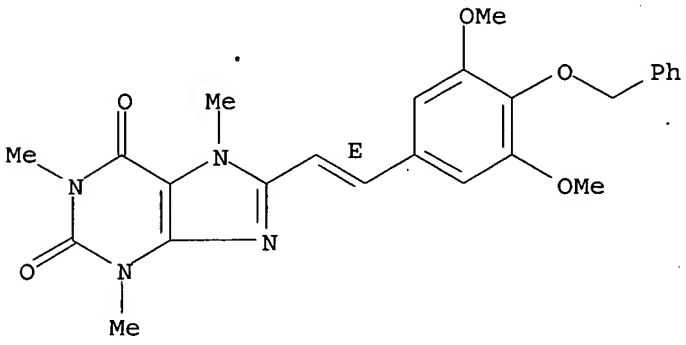
3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



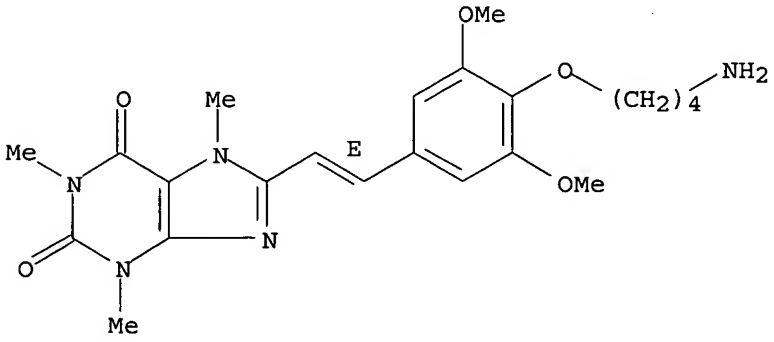
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



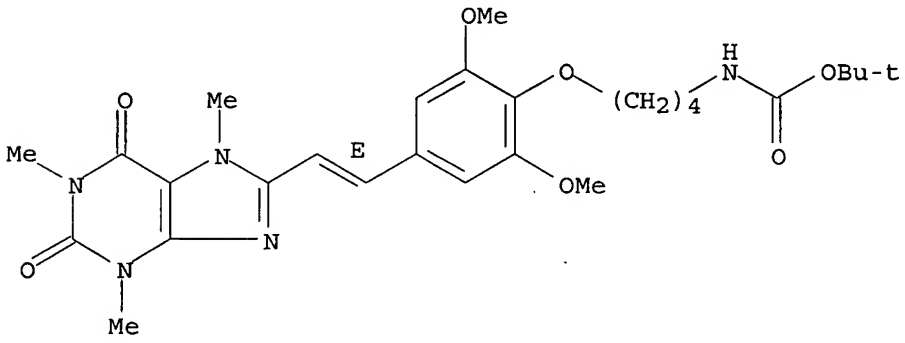
RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



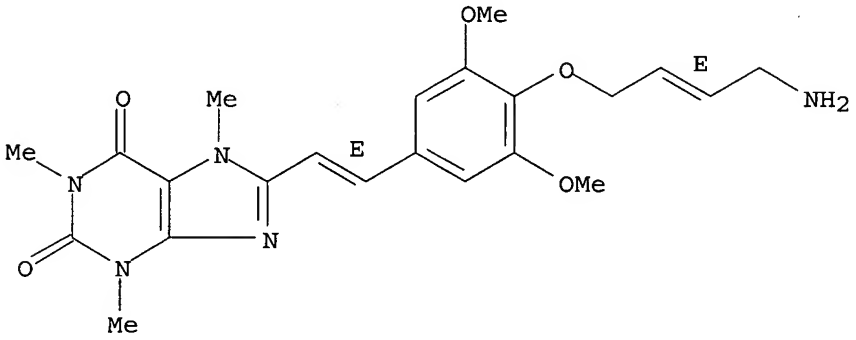
RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



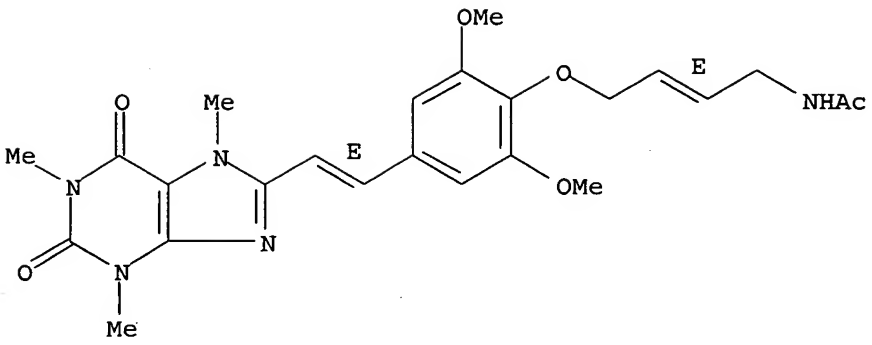
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



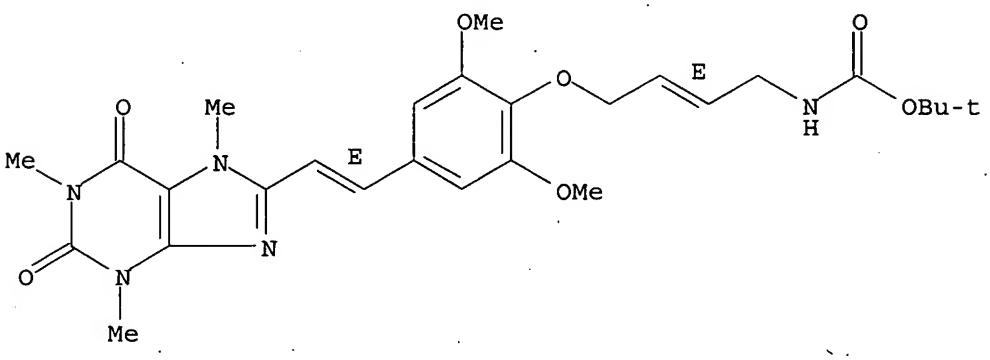
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



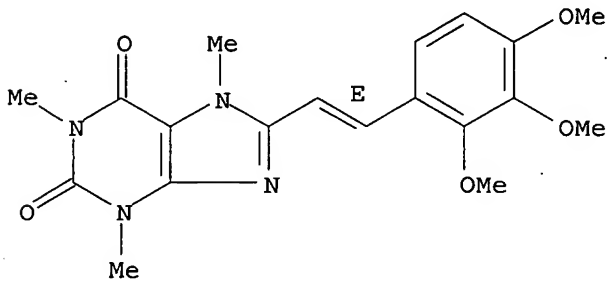
RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



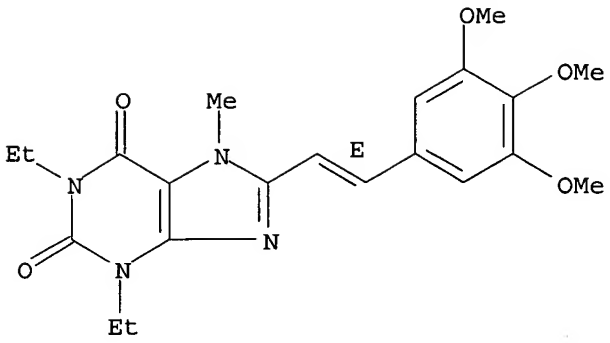
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:644563 HCAPLUS
DOCUMENT NUMBER: 130:33316
TITLE: Adenosine A2A receptors modify motor function in MPTP-treated common marmosets
AUTHOR(S): Kanda, Tomoyuki; Tashiro, Tomomi; Kuwana, Yoshihisa; Jenner, Peter
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co Ltd, Shizuoka, 411-8731, Japan
SOURCE: NeuroReport (1998), 9(12), 2857-2860
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both adenosine A1 and A2 receptor populations are located in the striatum and can modify locomotor activity, and they may form a therapeutic target for Parkinson's disease (PD). Administration of the selective adenosine A2A antagonist (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione (KW-6002) to MPTP-treated common marmosets increased locomotor activity. In contrast, administration of the selective A1 receptor antagonist 1,3-dipropyl-8-cyclopentylxantine (DPCPX) had no effect on locomotion. Administration of the adenosine A2A receptor agonist 2-[p-[2-(2-aminoethylamino) carbonylethyl] phenethyl amino]-5'-N-ethylcarboxamidoadenosine (APEC) dose dependently suppressed basal locomotor activity. A minimally ED of APEC (0.62 mg/kg, i.p) completely reversed the increase in locomotor activity produced by administration of KW-6002. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1, 14

IT **Brain**, disease
(basal ganglion; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT **Brain**
(corpus striatum; adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

IT **155270-99-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptors modify motor function in MPTP-treated common

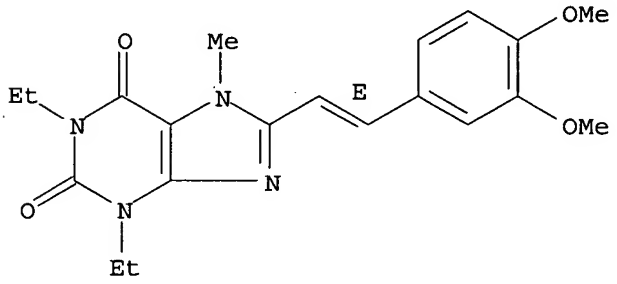
marmoset Parkinsonism model)

IT **155270-99-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(adenosine A2A receptors modify motor function in MPTP-treated common marmoset Parkinsonism model)

RN 155270-99-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-1,3-diethyl-3,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:394679 HCAPLUS

DOCUMENT NUMBER: 129:118143

TITLE: Pharmacological characterization of a simple behavioral response mediated selectively by central adenosine A1 receptors, using in vivo and in vitro techniques

AUTHOR(S): Marston, Hugh M.; Finlayson, Keith; Maemoto, Takuya; Olverman, Henry J.; Akahane, Atsushi; Sharkey, John; Butcher, Steven P.

CORPORATE SOURCE: Fujisawa Institute of Neuroscience, University of Edinburgh, Edinburgh, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(3), 1023-1030
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The behavioral profile of a range of adenosine receptor ligands was examined in rats using a locomotor activity model. Adenosine receptor agonists, including the selective A1 receptor agonist, N6-cyclopentyladenosine (CPA) and the A2A agonist, 2-[(2-aminoethylamino)carbonylethyl-phenylethylamino]-5'- ethylcarboxamidoadenosine (APEC), reduced spontaneous motor activity in a dose-dependent manner. CPA-induced locomotor depression was attenuated by adenosine A1 receptor selective antagonists, such as 8-cyclopentyl-1,3-dipropylxanthine (DPCPX), (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-2-piperidine ethanol (FK453), and (R)-1-[(E)-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-acryloyl]-piperidin-2-yl acetic acid (FK352), but not by the A2A receptor antagonist, (E)-1,3-dipropyl-8-(3,4-dimethoxystyryl)-7-methylxanthine (KF17837). By contrast, APEC-induced hypolocomotion was attenuated by KF17837 but not by

DPCPX, confirming that adenosine A1 and A2A receptor activation mediates locomotor output independently. Two peripheral adenosine receptor antagonists, 8-(p-sulfophenyl)-1,3-dipropylxanthine (DPSPX) and 8-(p-sulfophenyl)-1,3-dimethylxanthine (8-PST), did not alter CPA-induced hypolocomotion. This confirmed that pharmacol. reversal of the adenosine A1 receptor-mediated response involved a central site of drug action. The relationship between occupancy of central adenosine A1 receptors and behavioral effect was therefore assessed. Regression anal. on log transformed data confirmed assocns. between antagonist affinity for **brain** [3H]DPCPX binding sites and, in order of increasing significance, the equivalent behavioral dose (EBD) for reversal of CPA-induced hypolocomotion (R2 = 0.32), the serum concentration of drug (R2 = 0.65), and most significantly with the **brain** concentration of drug detected 20 min after administration of the (EBD) (R2 = 0.95). These data suggest that competition between agonists and antagonists, for occupancy of central adenosine A1 receptors, is intrinsic to the pharmacol. reversal of CPA-induced hypolocomotion. The validity of the model as a simple predictive screen for the blood/**brain** barrier permeability of adenosine A1 receptor antagonists was thereby confirmed.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1

ST adenosine A1 receptor locomotor behavior; blood **brain** barrier permeability A1 antagonist

IT Blood-**brain** barrier
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

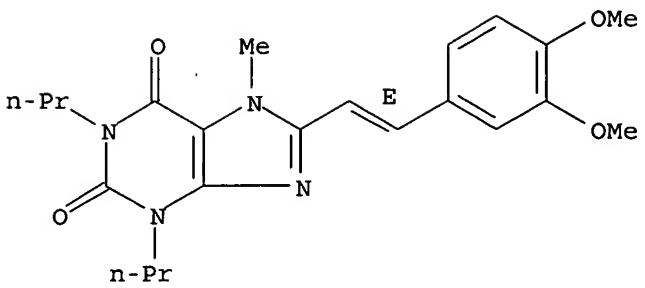
IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 146-77-0, 2-Chloroadenosine 961-45-5, 8-PT 35873-49-5, CPT 35920-39-9, 5'-N-Ethylcarboxamidoadenosine 36396-99-3 38594-96-6 41552-82-3, N6-Cyclopentyladenosine 75922-48-4, DPX 80206-91-3 89073-57-4 102146-07-6, DPCPX 121524-18-3, FK453 126828-50-0, APEC 136199-02-5, KW3902 137766-81-5, MDL102234 **141807-96-7**, KF17837 143881-08-7, FK352
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

IT **141807-96-7**, KF17837
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. characterization of behavioral response mediated selectively by central adenosine A1 receptors using in vivo and in vitro techniques in rats)

RN 141807-96-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:224850 HCAPLUS
DOCUMENT NUMBER: 128:267779
TITLE: Evaluation of carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand
AUTHOR(S): Noguchi, Junko; Ishiwata, Kiichi; Wakabayashi, Shin-Ichi; Nariai, Tadashi; Shumiya, Seigo; Ishii, Shin-Ichi; Toyama, Hinako; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio
CORPORATE SOURCE: Positron Medical Center and Department of Laboratory Animal Science, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173, Japan
SOURCE: Journal of Nuclear Medicine (1998), 39(3), 498-503
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 11C-labeled KF17837 ([7-methyl-11C](E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine) was evaluated as a PET ligand for mapping adenosine A2a receptors in the central nervous system (CNS). The regional **brain** distribution of [11C]KF17837 and the effect of adenosine antagonists on the distribution were measured in mice by the tissue sampling method. In rats, the regional **brain** uptake of [11C]KF17837 and the effect of carrier KF17837 was visualized by autoradiog. Imaging of the monkey **brain** with [11C]KF17837 was performed by PET. In mice, a high uptake of [11C]KF17837 was found in the striatum in which A2a receptors were highly enriched. The uptake was decreased by co-injection of carrier KF17837 or a xanthine-type A2a antagonist CSC but not by nonxanthine-type A2a antagonists ZM 241385 or SCH 58261, or an A1 antagonist KF15372. In the rat **brain**, [11C]KF17837 was accumulated higher in the striatum than in other **brain** regions, and the uptake was blocked by co-injection of carrier KF17837. In a monkey PET study, a high striatal uptake of radioactivity was observed Carbon-11-KF17837 binds to adenosine A2a receptors in the striatum. However, the presence of an unknown but specific binding site for xanthine-type compds. also was suggested in the other **brain** regions. The results also suggested that the in vivo receptor-binding sites of xanthine-type ligands are slightly different from those of nonxanthine-type A2a antagonists.

CC 8-9 (Radiation Biochemistry)
ST carbon 11 KF17837 adenosine receptor **brain**; PET imaging **brain** carbon 11 KF17837
IT **Brain**
Positron-emission tomography

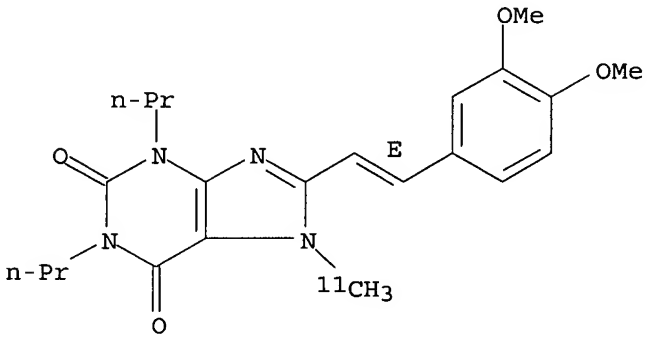
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(carbon-11-labeled KF17837: a potential CNS adenosine A2a receptor ligand)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:159025 HCAPLUS
DOCUMENT NUMBER: 130:322413
TITLE: Selective adenosine antagonists for mapping central nervous system adenosine receptors with positron emission tomography: carbon-11 labeled KF15372 (A1) and KF17837 (A2A)
AUTHOR(S): Suzuki, Fumio; Ishiwata, Kiichi
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, Japan
SOURCE: Drug Development Research (1998), 45(3/4), 312-323
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During the past decade, many neuroreceptors in humans and other animals have been visualized in vivo by positron emission tomog. (PET) with corresponding radioligands. Because adenosine is a neuromodulator, PET assessment of the adenosine receptor system offers us an opportunity to understand the neurotransmission system in general. The 11C-labeled selective adenosine A1 antagonists KF15372 and a 11C-Me derivative [11C]KF26345, and selective adenosine A2A antagonist KF17837 and KF18446

were evaluated in vivo as potential PET ligands for mapping CNS adenosine A1 and A2A receptors. [11C]KF15372 and [11C]KF263345: Tissue sampling and ex vivo autoradiog. (ARG) suggest that the regional **brain** distribution of [11C]KF15372 and [11C]KF26345 is consistent with that of the adenosine A1 receptors found in mice and rats. The **brain** uptake was competitively reduced by the coadministration of A1, but not by A2A antagonists. The ex vivo ARG on the rat model with unilateral orbital enucleation, visualized the A1 receptor deficiency in the presynaptic terminals. PET with these ligands visualized the A1 receptors in the monkey and cat **brain**. [11C]KF17837 and [11C]KF18446: In mice, a high uptake of two ligands was found in the striatum in which A2A receptors are highly enriched. The uptake was decreased by coinjection of carrier KF17837 or other xanthine-type A2A antagonists, but not by four nonxanthine-type A2A antagonists or A1 antagonists. In the rat **brain**, ex vivo ARG showed the A2A receptor-specific uptake of two ligands in the striatum. In PET studies of the monkey and cat **brain**, the A2A receptors in the striatum was clearly visualized. These pieces of evidence demonstrated the potential of 11C-labeled selective xanthine-type adenosine antagonists as PET ligands for mapping CNS adenosine A1 and A2A receptors.

CC 8-9 (Radiation Biochemistry)

IT **Brain**
Positron-emission tomography
Purinoceptor antagonists
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

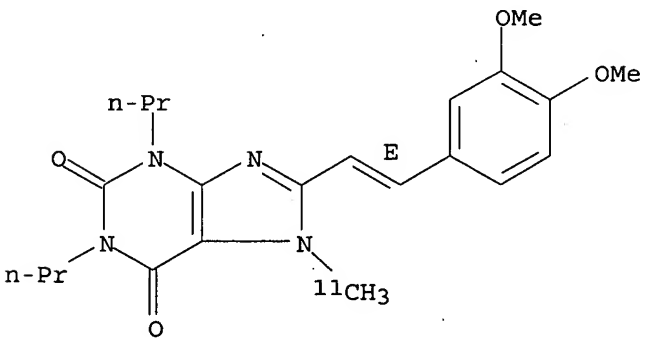
IT 170660-22-7 **179678-39-8** 188486-06-8 **223745-98-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

IT **179678-39-8 223745-98-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(adenosine antagonists for mapping central nervous system adenosine receptors with PET)

RN 179678-39-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

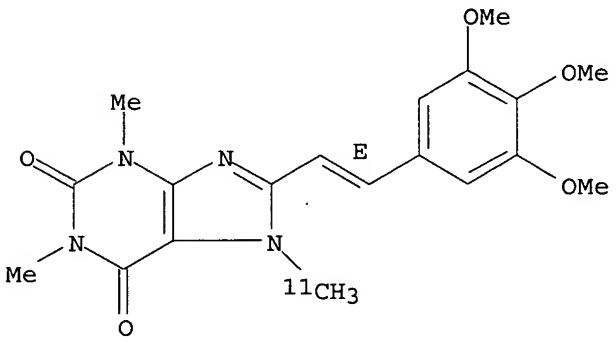
Double bond geometry as shown.



RN 223745-98-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(methyl-11C)-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 31 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:3847 HCAPLUS
DOCUMENT NUMBER: 128:85873
TITLE: In vivo evaluation of [11C]KF17837, a selective adenosine A2a antagonist, for mapping of CNS adenosine A2a receptor
AUTHOR(S): Noguchi, J.; Ishiwata, K.; Ishii, S.; Koike, N.; Wakabayashi, S.; Nariai, T.; Endo, K.; Suzuki, F.; Senda, M.
CORPORATE SOURCE: Positron Med. Cent., Tokyo Metropolitan Inst. Gerontol., Tokyo, 173, Japan
SOURCE: International Congress Series (1997), 1140(Role of Adenosine in the Nervous System), 201-206
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The carbon-11-labeled KF17837 ([7-methyl-11C](E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine) was evaluated as a radioligand for mapping adenosine A2a receptors in the central nervous system (CNS) by positron emission tomog. (PET). In mice, a high uptake of [11C]KF17837 was found in the striatum in which A2a receptors are highly enriched. The uptake was decreased by co-injection of carrier KF17837 or a xanthine type A2a antagonist CSC, but not by non-xanthine type A2a antagonists ZM 241385 or an A1 antagonist KF15372. In the rat **brain**, [11C]KF17837 accumulated higher in the striatum than in other **brain** regions and the uptake was blocked by co-injection of carrier KF17837. In a monkey PET study, a high striatal uptake of radioactivity was observed These pieces of evidence have demonstrated the potential of [11C]KF17837 as a PET ligand for mapping adenosine A2a receptors in the CNS.

CC 8-9 (Radiation Biochemistry)

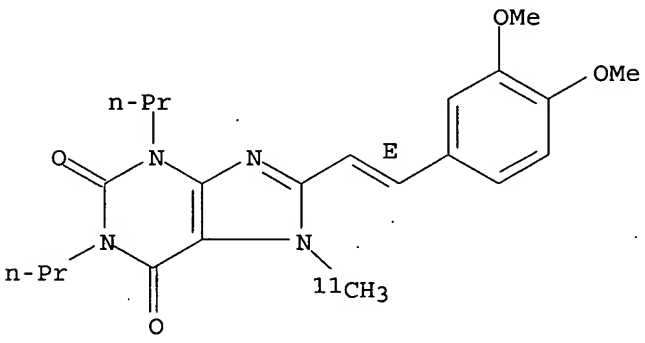
IT **Brain**
Positron-emission tomography
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified);

decreased more rapidly in the cortex than in the striatum and cerebellum (by 20% vs. 3-7%, resp., between 5 and 50 min). Addition of carrier to [N-11C-methyl]KF 17837 only marginally affected the cerebral radiotracer uptake. By contrast, in the heart the initial tracer uptake was high and the elimination kinetics was enhanced by adding unlabeled carrier. We have thus shown that KF 17837 passes the blood-**brain** barrier, though to a very low extent. This fact and the apparently high nonspecific binding in vivo of [N-11C-methyl]KF 17837 in regions with low receptor densities limits its usefulness as a ligand for quantification of the adenosine A2A receptors in the primate **brain**.

CC 8-9 (Radiation Biochemistry)
ST **brain** adenosine receptor PET; carbon 11 KF 17837 PET
IT **Brain**
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of **brain** adenosine A2A receptors)
IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of adenosine A2A receptors)
IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
([N-11C-methyl]KF 17837 biodistribution using 3-D-PET: evaluation as ligand for study of adenosine A2A receptors)
RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



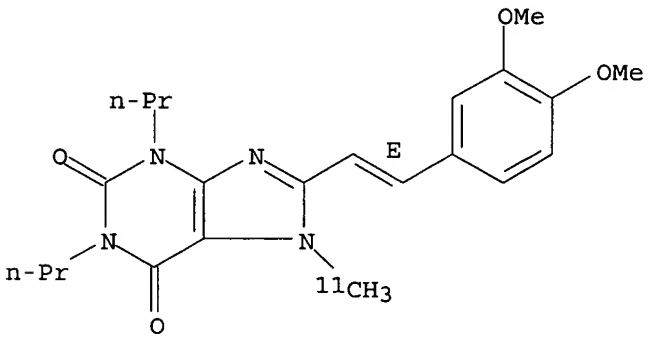
L34 ANSWER 33 OF 40 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97364156 EMBASE
DOCUMENT NUMBER: 1997364156
TITLE: Adenosine A(2A) receptors and neuroprotection.
AUTHOR: Ongini E.; Adami M.; Ferri C.; Bertorelli R.
CORPORATE SOURCE: E. Ongini, Schering-Plough Research Institute, San Raffaele Science Park, Via Olgettina 58, I-20132 Milan, Italy
SOURCE: Annals of the New York Academy of Sciences, (1997) Vol. 825, pp. 30-48.
Refs: 86

THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)

IT **179678-39-8**
RL: BPR (Biological process); BSU (Biological study, unclassified);
THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
([11C]KF17837 in vivo evaluation as PET ligand for mapping of CNS adenosine A2a receptor)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:237596 HCAPLUS
DOCUMENT NUMBER: 126:261014
TITLE: In vivo biodistribution of [N-11C-methyl]KF 17837 using 3-D-PET: evaluation as a ligand for the study of adenosine A2A receptors
AUTHOR(S): Stone-Elander, Sharon; Thorell, Jan-Olov; Eriksson, Lars; Fredholm, Bertil B.; Ingvar, Martin
CORPORATE SOURCE: KAROLINSKA PHARMACY, STOCKHOLM, S-17176, Swed.
SOURCE: Nuclear Medicine and Biology (1997), 24(2), 187-191
CODEN: NMBIEO; ISSN: 0883-2897
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KF 17837, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine, was 11C-labeled by methylation at N-7 of the nor-compound, KF 17440, using [11C]methyl iodide. Radiochem. conversions of 50% or 70-80% were obtained using sodium hydride or potassium carbonate, resp., as base. Total synthesis time was 40-45 min, including isolation by semipreparative liquid chromatog. Cerebral uptake of [N-11C-methyl]KF 17837 in Cynomolgus monkeys, evaluated using positron emission tomog. (PET), was so low that regional differences in distribution kinetics were revealed first after increasing injected dose 3-fold and using 3-D mode of data acquisition. At all times, the relative regional retention (maximum striatum:cerebellum: cortex ≈ 1.1:1:0.8 at 20 min) was considerably different from the known relative d. of A2A receptors in these regions. Radioactivity

ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 971218
Last Updated on STN: 971218

AB The adenosine A(2A) receptor subtype is one of the four adenosine receptors that have been identified in the mammalian organism. In addition to being found in blood vessels, platelets and polymorphonuclear leukocytes, the A(2A) receptors are abundant in the central nervous system, especially in the striatum. The recent development of selective A(2A) receptor ligands, in particular of receptor antagonists, makes it possible to elucidate the function of A(2A) receptors in normal and altered conditions. Pharmacological studies have shown that A(2A) receptor antagonists are potentially effective for treatment of neurodegenerative processes such as Parkinson's disease. Their activity is attributed to the close anatomical and functional links between A(2A) receptors and dopaminergic pathways in the basal ganglia. More recently, A(2A) receptor antagonists have proved to be active in models of cerebral ischemia. While the mechanisms underlying the role of A(2A) receptors in the hypoxia/ischemia processes remains to be clarified, it is recognized that A(2A) receptor antagonists counteract the effects of excitatory aminoacids, which are massively released after cerebral ischemia. Another function of A(2A) receptors is related to protection from seizures, but further studies are needed to elucidate their specific interaction, if any, with neuronal excitability. Altogether, the great advance recently made with the discovery of selective A(2A) receptor ligands provides increasing information on the function of A(2A) receptors and opens new perspectives for treatment of neurological disorders.

CT Medical Descriptors:
*neuroprotection
brain ischemia: ET, etiology
complex partial seizure: ET, etiology
conference paper
drug selectivity
drug structure
human
nonhuman
parkinson disease: ET, etiology
structure activity relation
Drug Descriptors:
*adenosine a2a receptor: EC, endogenous compound
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): DV, drug development
2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide): PD, pharmacology
4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline: DV, drug development
4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline: PD, pharmacology
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: DV, drug development
5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine: PD, pharmacology
8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: PD, pharmacology

8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine: DV, drug development
9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline: DV, drug development
9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline: PD, pharmacology
adenosine 5' (n ethylcarboxamide): DV, drug development
adenosine 5' (n ethylcarboxamide): PD, pharmacology
adenosine a2a receptor agonist: DV, drug development
caffeine: PD, pharmacology
dizocilpine

RN (2 [4 (2 carboxyethyl)phenethylamino]adenosine 5' (n ethylcarboxamide)) 120225-54-9; (4 amino 8 chloro 1 phenyl 1,2,4 triazolo[4,3 a]quinoxaline) 91896-57-0; (5 amino 2 (2 furyl) 7 (2 phenylethyl)pyrazolo[4,3 e][1,2,4]triazolo[1,5 c]pyrimidine) 160098-96-4; (8 (3,4 dimethoxystyryl) 7 methyl 1,3 dipropylxanthine) **141807-96-7**; (9 chloro 2 (2 furyl) 5,6 dihydro 5 imino 1,2,4 triazolo[2,3 c]quinazoline) 104615-18-1; (adenosine 5' (n ethylcarboxamide)) 35920-39-9; (caffeine) 30388-07-9, 58-08-2; (dizocilpine) 77086-21-6

CN Cgs 21680; Kf 17837; Sch 58261; Cp 66713; Cgs 15943; Mk 801

L34 ANSWER 34 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:701996 HCAPLUS
DOCUMENT NUMBER: 126:1192
TITLE: Methods for protecting tissues and organs from ischemic damage
INVENTOR(S): Downey, James M.; Mullane, Kevin M.
PATENT ASSIGNEE(S): Gensia, Inc., USA; South Alabama Medical Science Foundation
SOURCE: U.S., 16 pp., Cont.-in-part of U.S. 5, 443, 836.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5573772	A	19961112	US 1994-214942	19940317
US 5443836	A	19950822	US 1993-33310	19930315
PRIORITY APPLN. INFO.:			US 1993-33310 A2	19930315

AB Methods for protecting tissues and organs including the heart central nervous system, and kidney from ischemic damage are described and claimed based upon the recognition that protection against infarction is mediated by A3 rather than A1 adenosine receptors, as was previously thought, and that the receptor mediating protection in other organs and tissues has not been defined. Methods for selectively stimulating A3 adenosine receptors are described and claimed, as such selection is shown to prevent or substantially reduce cell death resulting from ischemia with or without reperfusion in humans. According to this invention, the A3 adenosine receptor is selectively stimulated by administering a compound which is an A3 adenosine receptor-selective agonist. Prevention of tissue death is also achieved by administering a compound which is a non-selective adenosine receptor agonist together with compds. that act as antagonists to the A1 and A2 adenosine receptor.

IC ICM A61F002-02
ICS A61K009-48; A61K009-20; A61K009-14
INCL 424423000
CC 1-8 (Pharmacology)

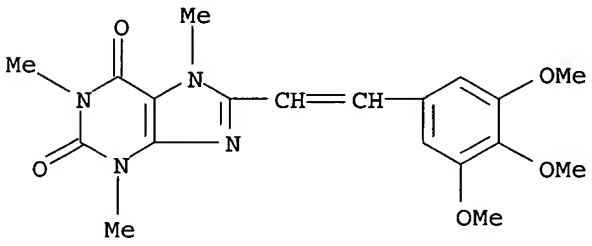
Section cross-reference(s): 63

IT **Brain, disease**
Heart, disease
Kidney, disease
(**ischemia**, preconditioning; methods for protecting tissues and organs from ischemic damage)

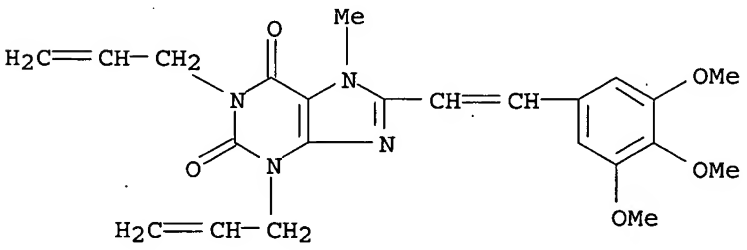
IT **31377-36-3** 36396-99-3 37739-05-2, 2-Chloro-N6-cyclopentyladenosine 38594-97-7 41552-82-3, N6-Cyclopentyladenosine 96865-92-8, XAC 97905-57-2 98866-49-0 102146-07-6, Dpcpx 105834-00-2 116370-30-0, BW-A844U 120225-54-9, CGS 21680 124498-52-8, CGS 22492 124498-87-9, CGS 22989 131080-42-7, KF 15372 131933-18-1 133058-72-7, KFM 19 141696-90-4, N-0861 **158962-89-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for protecting tissues and organs from ischemic damage)

IT **31377-36-3 158962-89-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for protecting tissues and organs from ischemic damage)

RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



L34 ANSWER 35 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:368146 HCAPLUS
DOCUMENT NUMBER: 125:142663
TITLE: Synthesis and preliminary evaluation of [11C]KF17837,

a selective adenosine A2A antagonist

AUTHOR(S): Ishiwata, Kiichi; Noguchi, Junko; Toyama, Hinako; Sakiyama, Yojiro; Koike, Nobuaki; Ishii, Shin-Ichi; Oda, Keiichi; Endo, Kazutoyo; Suzuki, Fumio; Senda, Michio

CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Inst. Gerontology, Tokyo, 173, Japan

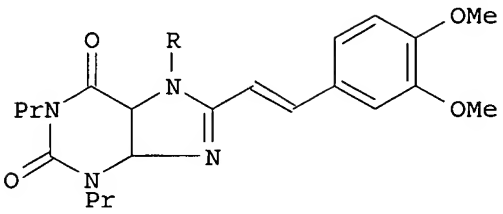
SOURCE: Applied Radiation and Isotopes (1996), 47(5/6), 507-511
CODEN: ARISEF; ISSN: 0969-8043

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB An 11C-labeled selective adenosine A2A antagonist, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-[11C]methylxanthine (I; R = 11CH3; [11C]KF17837), was prepared by reactions of (E)-8-(3,4-dimethoxystyryl)-1,3-dipropylxanthine (I; R = H)and [11C]methyl iodide with decay-corrected radiochem. yield of 19-50%, radiochem. purity of >99%, sp. act. of 17-100 GBq/μ mol and preparation time of 20-25 min. In mice, the myocardium showed the highest (13.4% ID/g) at at 5 min after i.v. injection, which decreased gradually with time. The specific myocardial uptake was visualized by γ-camera. In the **brain** region the radioactivity level was higher in the A2A receptors-rich striatum than in the cortex and cerebellum. The specific striatal uptake in rats was clearly demonstrated by PET. These results shown that [11C]KF17837 is a potential PET radioligand for mapping the adenosine A2A receptors in the heart and **brain**.

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST KF17837 radiolabeled prepn adenosine receptor antagonist; dimethoxystyrylmethylxanthine radiolabeled prepn adenosine receptor antagonist; dimethoxystyryldipropylxanthine alkylation radiolabeled methyl iodide; heart bioavailability radiolabeled KF17837; **brain** bioavailability radiolabeled KF17837; myocardium bioavailability radiolabeled KF17837; cortex bioavailability radiolabeled KF17837; cerebellum bioavailability radiolabeled KF17837; striatal uptake radiolabeled KF17837; PET radioligand KF17837 prepn

IT Animal tissue
Brain
Heart
(synthesis and biodistribution of [11C]KF17837 in)

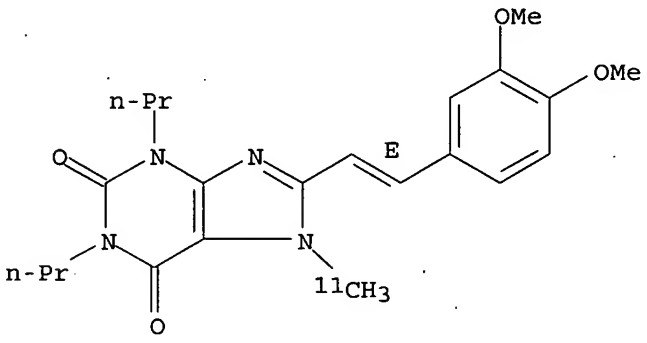
IT **179678-39-8P**, [7-11C]-(E)-8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and preliminary evaluation of [11C]KF17837 as a adenosine A2A antagonist)

IT **179678-39-8P**, [7-11C]-(E)-8-(3,4-Dimethoxystyryl)-1,3-dipropyl-7-methylxanthine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and preliminary evaluation of [11C]KF17837 as a adenosine A2A antagonist)

RN 179678-39-8 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-(methyl-11C)-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

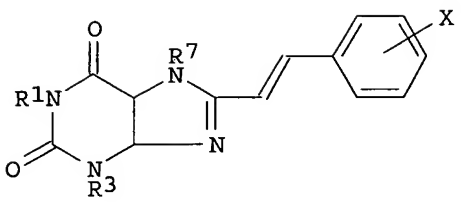


L34 ANSWER 36 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:446631 HCAPLUS
DOCUMENT NUMBER: 122:213859
TITLE: Preparation of 8-styryl-1,3,7-trialkylxanthine derivatives as A2-selective adenosine receptor antagonists
INVENTOR(S): Jacobson, Kenneth A.; Karton, Yishai; Gallo-Rodriguez, Carola; Fischer, Bilha; Van Galen, Philip J. M.; Maillard, Michel
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9425462	A1	19941110	WO 1994-US4876		19940503
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9467811	A1	19941121	AU 1994-67811		19940503
US 5861405	A	19990119	US 1994-335108		19941107
PRIORITY APPLN. INFO.:			US 1993-57086	A	19930503
			WO 1994-US4876	W	19940503

OTHER SOURCE(S): MARPAT 122:213859

GI



I

AB Title compds. (I; R1, R3, R7 = Me; X = 1-3 of amino, acylamino, diacylamino, halo, alkoxy, aminoalkoxy, aminoalkenyloxy, isothiocyanato, diazonium), and related compds., were prepared Thus, 1,3,7-trimethyl-8-(2-methoxystyryl)xanthine, prepared from 2-methoxycinnamic acid, showed Ki = 4760 nM and 267 nM for binding rat **brain** A1 and A2a receptors, resp.

IC ICM C07D473-08
ICS C07D473-12; C07D473-06; A61K031-52

CC 26-9 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 147700-11-6P 147700-24-1P **147700-25-2P 147700-30-9P 147700-31-0P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(adenosine receptor antagonist activity)

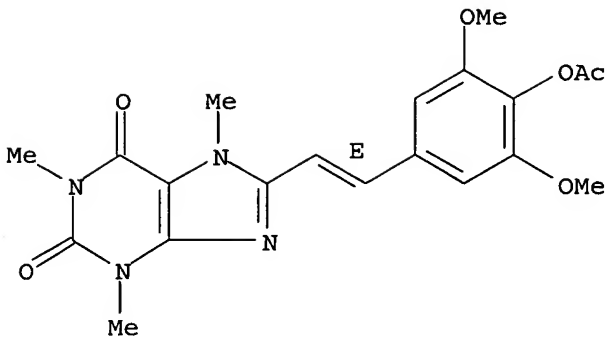
IT **51389-37-8P** 99765-13-6P 141807-86-5P **141807-96-7P**
147699-95-4P 147699-98-7P 147700-00-3P 147700-02-5P 147700-04-7P
147700-05-8P 147700-06-9P 147700-07-0P 147700-08-1P 147700-10-5P
147700-13-8P 147700-15-0P 147700-17-2P **147700-19-4P**
147700-21-8P 147700-23-0P **147700-26-3P 147700-27-4P**
147700-28-5P 147700-29-6P 147700-33-2P
147700-35-4P 147700-36-5P 147700-37-6P
147700-38-7P 147700-40-1P 147700-41-2P 147700-42-3P
147700-44-5P 147700-46-7P 147700-50-3P **147700-52-5P**
147700-54-7P 147700-55-8P 151539-31-0P 161826-76-2P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-styryl-1,3,7-trialkylxanthine derivs. as A2-selective adenosine receptor antagonists)

IT **147700-25-2P 147700-30-9P 147700-31-0P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(adenosine receptor antagonist activity)

RN 147700-25-2 HCAPLUS

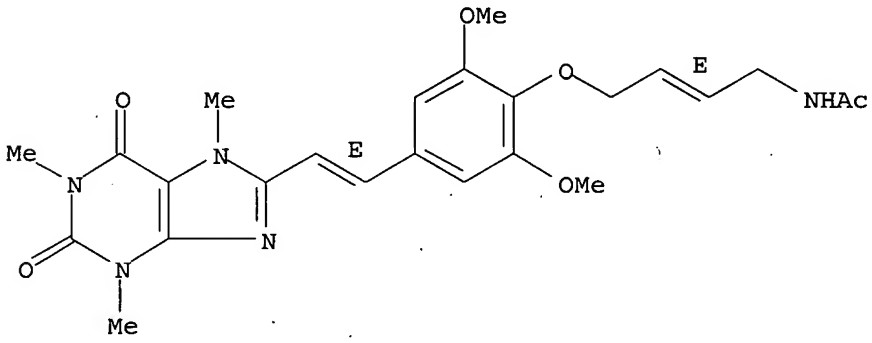
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(acetyloxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



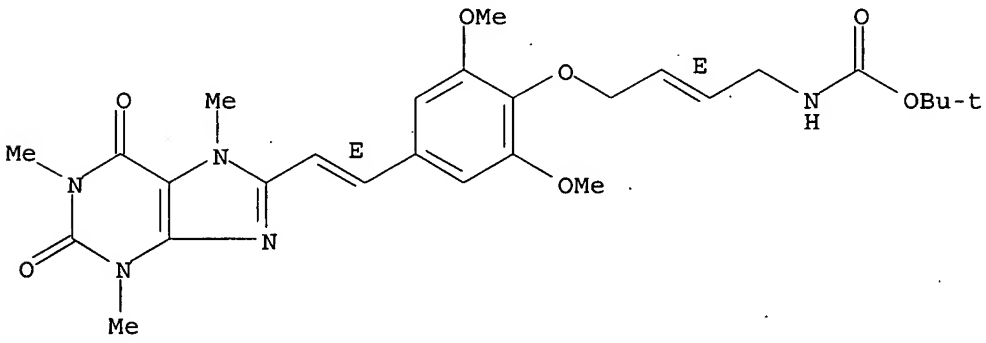
RN 147700-30-9 HCAPLUS
CN Acetamide, N-[(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-31-0 HCAPLUS
CN Carbamic acid, [(2E)-4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

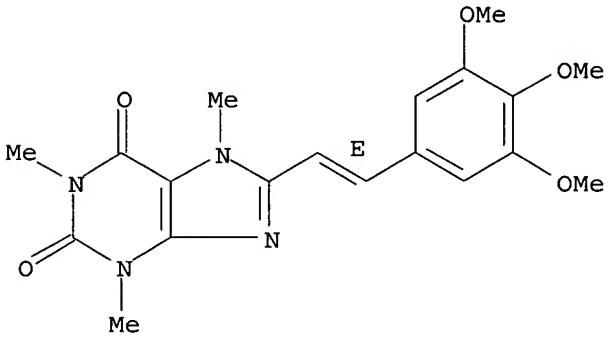


IT **51389-37-8P 141807-96-7P 147700-19-4P**
147700-26-3P 147700-27-4P 147700-28-5P
147700-29-6P 147700-33-2P 147700-35-4P

147700-36-5P 147700-37-6P 147700-38-7P
147700-40-1P 147700-52-5P 147700-54-7P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-styryl-1,3,7-trialkylxanthine derivs. as A2-selective adenosine receptor antagonists)

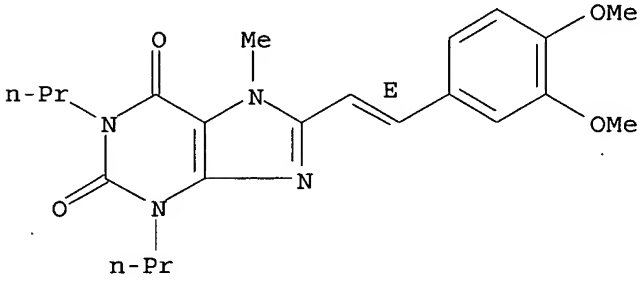
RN 51389-37-8 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



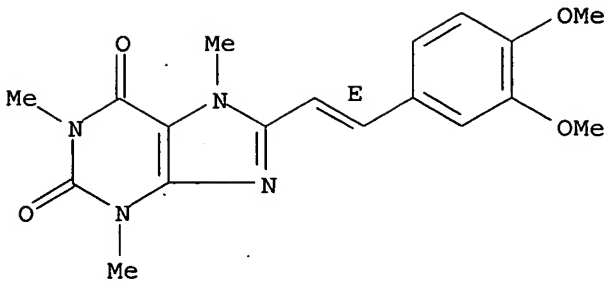
RN 141807-96-7 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



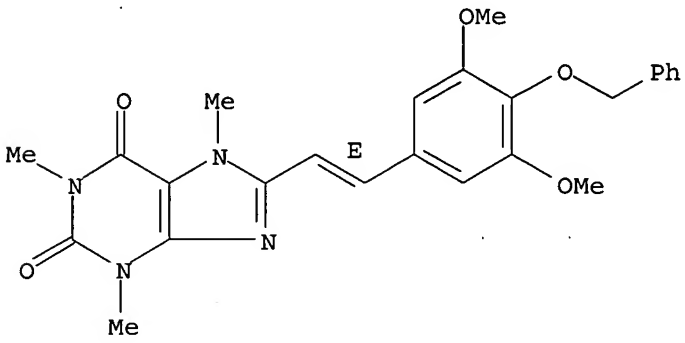
RN 147700-19-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



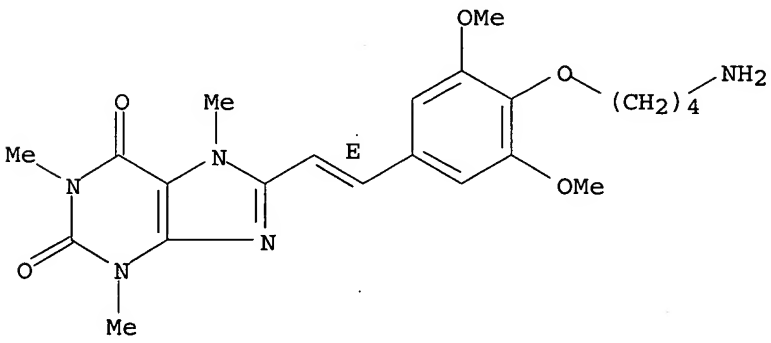
RN 147700-26-3 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[3,5-dimethoxy-4-(phenylmethoxy)phenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



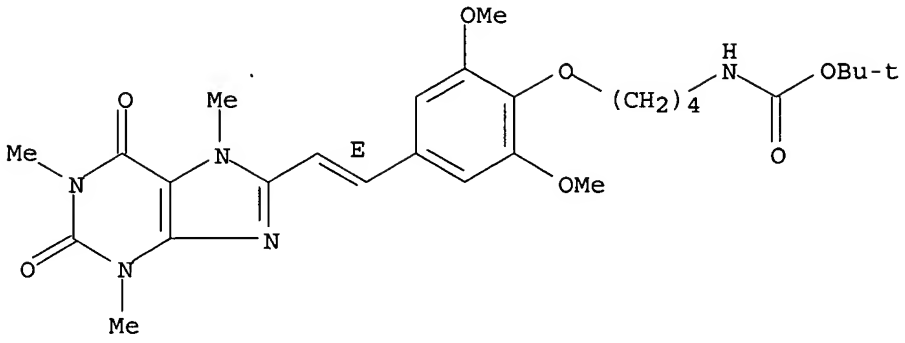
RN 147700-27-4 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-(4-aminobutoxy)-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



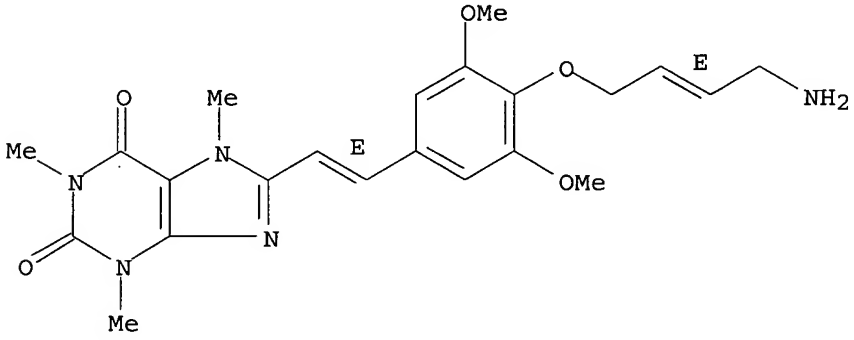
RN 147700-28-5 HCAPLUS
CN Carbamic acid, [4-[2,6-dimethoxy-4-[(1E)-2-(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)ethenyl]phenoxy]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



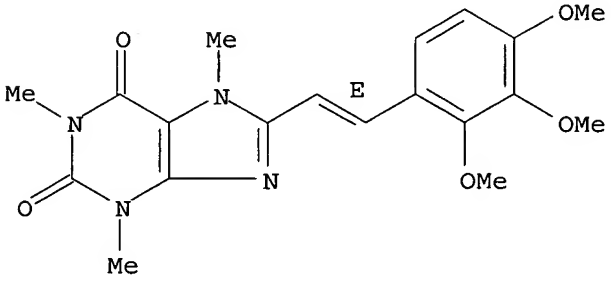
RN 147700-29-6 HCAPLUS
CN 1H-Purine-2,6-dione, 8-[(1E)-2-[4-[[(2E)-4-amino-2-butenyl]oxy]-3,5-dimethoxyphenyl]ethenyl]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



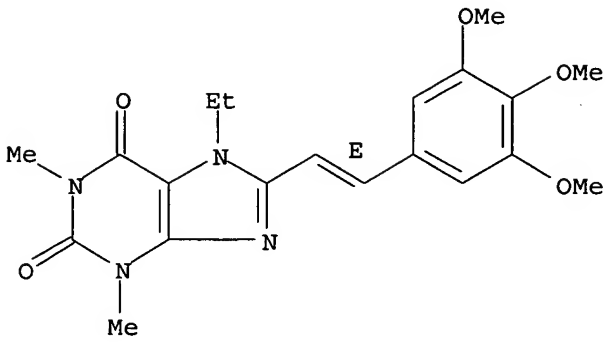
RN 147700-33-2 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(1E)-2-(2,3,4-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



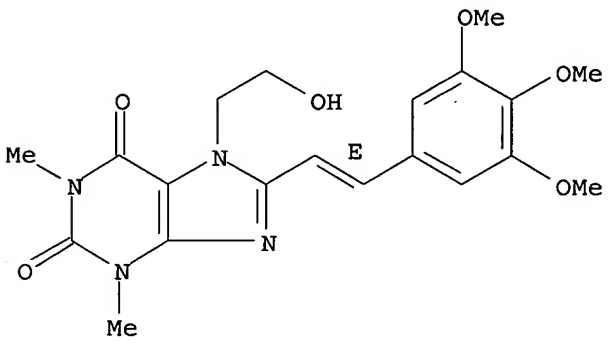
RN 147700-35-4 HCAPLUS
CN 1H-Purine-2,6-dione, 7-ethyl-3,7-dihydro-1,3-dimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



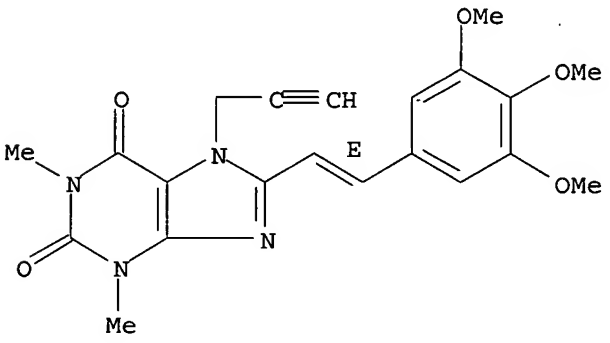
RN 147700-36-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-(2-hydroxyethyl)-1,3-dimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



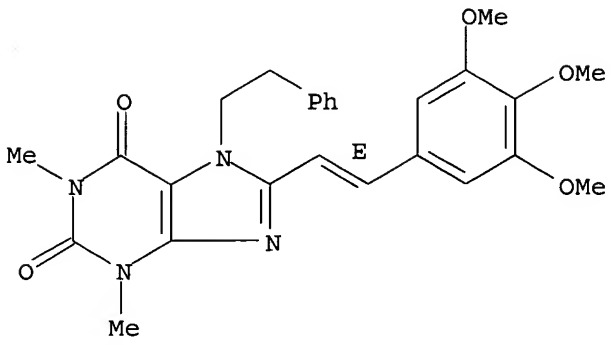
RN 147700-37-6 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(2-propynyl)-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



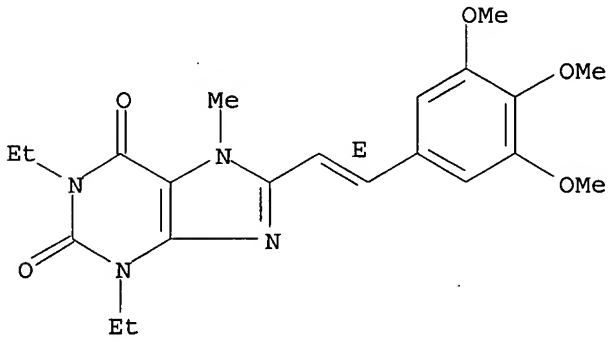
RN 147700-38-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(2-phenylethyl)-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



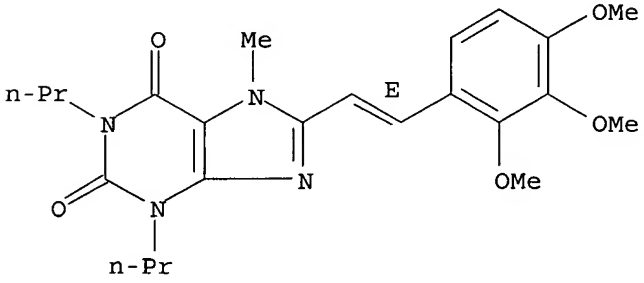
RN 147700-40-1 HCAPLUS
CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-7-methyl-8-[(1E)-2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



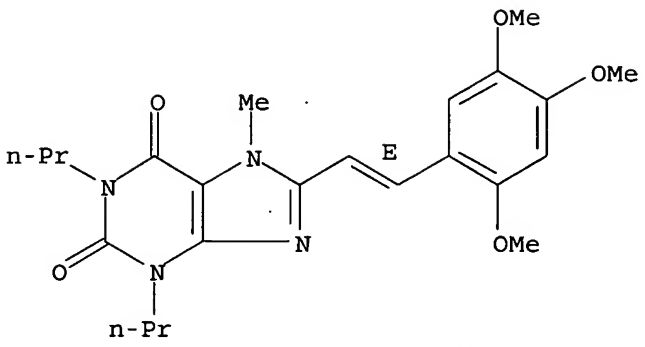
RN 147700-52-5 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-dipropyl-8-[2-(2,3,4-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 147700-54-7 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-dipropyl-8-[2-(2,4,5-trimethoxyphenyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



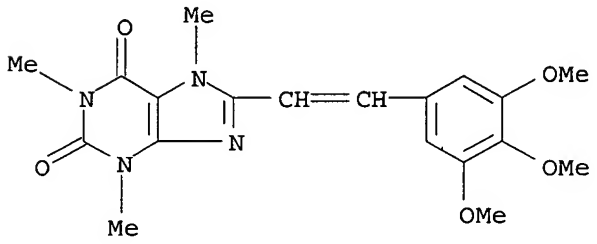
L34 ANSWER 37 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:672194 HCAPLUS
DOCUMENT NUMBER: 121:272194
TITLE: Methods for protecting tissues and organs from ischemic damage
INVENTOR(S): Downey, James M.; Mullane, Kevin M.
PATENT ASSIGNEE(S): Gensia, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421195	A1	19940929	WO 1994-US2854	19940315
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5443836	A	19950822	US 1993-33310	19930315
AU 9463662	A1	19941011	AU 1994-63662	19940315
EP 689405	A1	19960103	EP 1994-910956	19940315
R: CH, DE, FR, GB, IT, LI, NL				

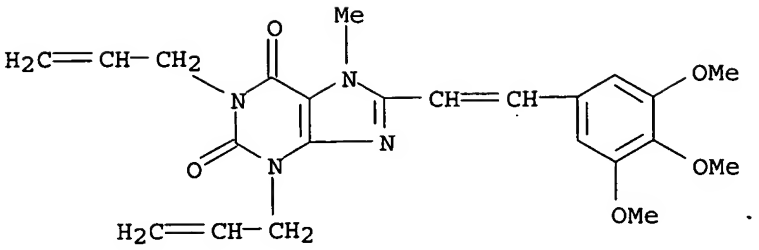
PRIORITY APPLN. INFO.:	US 1993-33310	A	19930315
	WO 1994-US2854	W	19940315

AB Methods for protecting tissues and organs including the heart, central nervous system, and kidney from ischemic damage are described and claimed based upon the recognition that protection against infarction is mediated by A3 rather than A1 adenosine receptors, as was previously thought, and that the receptor mediating protection in other organs and tissues has not been defined. Methods for selectively stimulating A3 adenosine receptors are described and claimed, as such selection is shown to prevent or substantially reduce cell death resulting from ischemia with or without reperfusion in humans. According to this invention, the A3 adenosine receptor is selectively stimulated by administering a compound which is an A3 adenosine receptor-selective agonist. Prevention of tissue death is also achieved by administering a compound which is a non-selective adenosine receptor agonist together with compds. that act as antagonists to the A1 and A2 adenosine receptor.

IC ICM A61F002-02
ICS A61K009-14; A61K009-20; A61K009-48; A61M031-00
CC 1-12 (Pharmacology)
ST A3 adenosine receptor agonist; A1 adenosine receptor antagonist; A2 adenosine receptor antagonist; ischemic damage organ; **brain** heart kidney ischemic damage
IT **Ischemia**
(organ; A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT **Brain, disease**
Heart, disease
Kidney, disease
(**ischemia**, A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT 58-61-7, Adenosine, biological studies **31377-36-3** 35920-39-9, 5'-N-Ethylcarboxamidoadenosine 38594-96-6 102146-07-6, 1,3-Dipropyl-8-cyclopentylxanthine 105834-00-2 116370-30-0, BW-A 844U 131080-42-7, KF 15372 133058-72-7, KFM 19 141696-90-4, N-0861 152918-15-5 152918-16-6 152918-17-7 152918-18-8 158962-88-0 **158962-89-1**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
IT **31377-36-3 158962-89-1**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(A3 adenosine receptor agonists, and A1 and A2 adenosine receptor antagonists are used for protecting tissue and organs from ischemic damage)
RN 31377-36-3 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 158962-89-1 HCAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-methyl-1,3-di-2-propenyl-8-[2-(3,4,5-trimethoxyphenyl)ethenyl]- (9CI) (CA INDEX NAME)

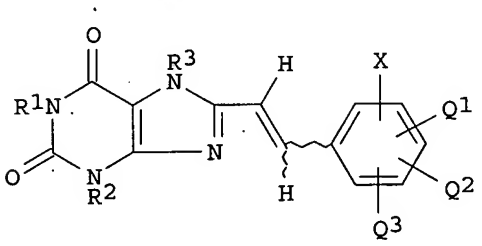


L34 ANSWER 38 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:168999 HCAPLUS
DOCUMENT NUMBER: 122:81388
TITLE: (Styryl)xanthine-derivatives adenosine A2 receptor antagonists
INVENTOR(S): Suzuki, Fumio; Shimada, Junichi; Koike, Nobuaki; Kase, Hiroshi; Nakamura, Joji; Shiozaki, Shizaki; Nonaka, Hiromi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Can. Pat. Appl., 69 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2112031	AA	19940625	CA 1993-2112031	19931221
JP 06239862	A2	19940830	JP 1993-316132	19931216
JP 3165769	B2	20010514		
NO 9304792	A	19940627	NO 1993-4792	19931223
EP 607607	A1	19940727	EP 1993-120842	19931223
EP 607607	B1	19960918		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 143019	E	19961015	AT 1993-120842	19931223
US 5670498	A	19970923	US 1995-527497	19950913

PRIORITY APPLN. INFO.: JP 1992-344116 A 19921224
US 1993-171602 B1 19931222

OTHER SOURCE(S): MARPAT 122:81388
GI



I

AB The title compds. [I; Q1-Q3 = H, lower alkyl, lower alkoxy, halogen; R1-R3 = H, lower alkyl; X = COR4, SO2R5; R4 = H, HO, lower alkyl, lower alkoxy; R5 = (un)substituted NH2, etc.], useful as adenosine A2 receptor

antagonists for the treatment of Parkinson's disease (no data), depression (no data), etc., are prepared and I-containing formulations presented. Thus, (E)-8-(3-acetylstyryl)-1,3-diethyl-7-methylxanthine, m.p. 221.4-221.8°, was prepared and demonstrated 85% inhibition. of 3H-CGS 21680 binding to rat **brain**-derived adenosine A2 receptors at 10-7 mol (Ki = 13 nM).

IC ICM C07D473-04
ICS A61K031-52

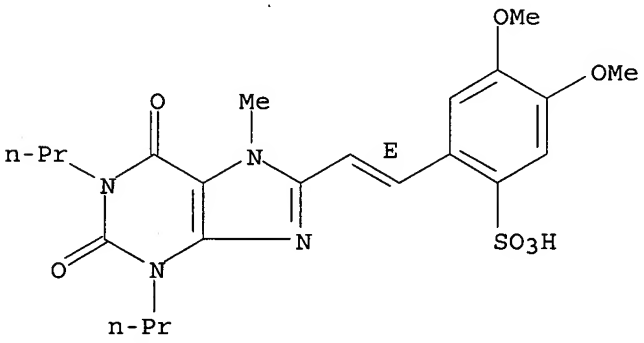
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **160434-09-3P 160434-10-6P 160434-11-7P**
160434-12-8P 160434-14-0P 160434-15-1P
160434-16-2P 160434-17-3P **160434-18-4P 160434-19-5P**
160434-20-8P 160434-21-9P 160434-23-1P
160434-24-2P 160434-25-3P 160434-26-4P 160434-27-5P
160434-28-6P 160434-29-7P 160434-30-0P 160434-31-1P 160434-32-2P
160434-33-3P 160434-34-4P 160434-35-5P 160434-36-6P 160434-37-7P
160434-38-8P 160434-39-9P 160434-40-2P 160471-61-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(styrylxanthine adenosine A2 receptor antagonists)

IT **160434-09-3P 160434-10-6P 160434-11-7P**
160434-12-8P 160434-14-0P 160434-15-1P
160434-18-4P 160434-19-5P 160434-20-8P
160434-21-9P 160434-23-1P 160434-24-2P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(styrylxanthine adenosine A2 receptor antagonists)

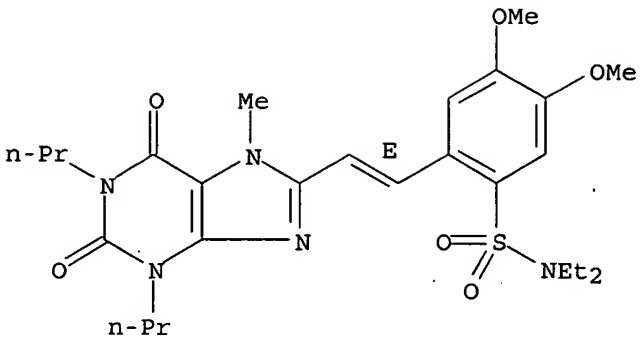
RN 160434-09-3 HCAPLUS
CN Benzenesulfonic acid, 4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



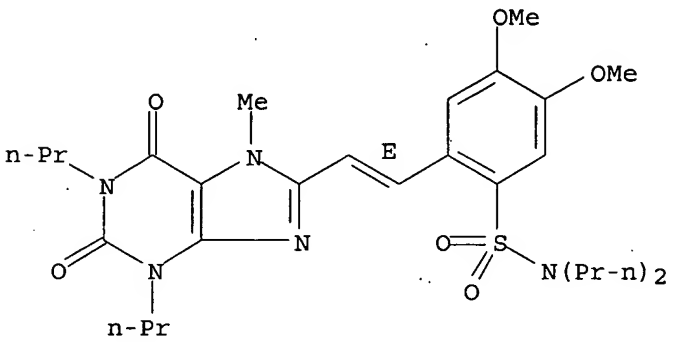
RN 160434-10-6 HCAPLUS
CN Benzenesulfonamide, N,N-diethyl-4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



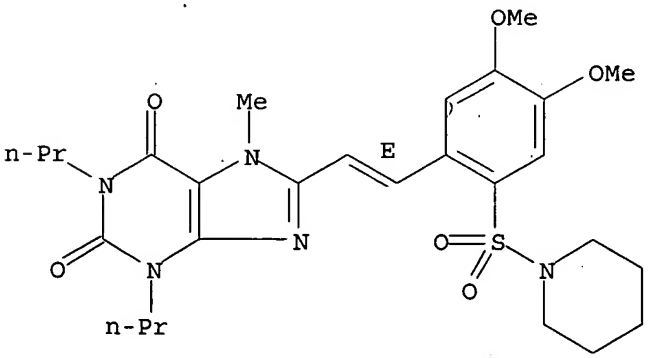
RN 160434-11-7 HCAPLUS
CN Benzenesulfonamide, 4,5-dimethoxy-N,N-dipropyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 160434-12-8 HCAPLUS
CN Piperidine, 1-[[4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]phenyl]sulfonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



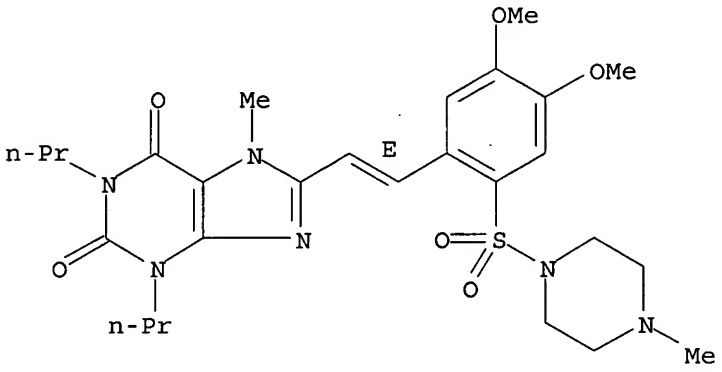
RN 160434-14-0 HCAPLUS
CN Piperazine, 1-[[4,5-dimethoxy-2-[(1E)-2-(2,3,6,7-tetrahydro-7-methyl-2,6-

dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]phenyl]sulfonyl]-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 160434-13-9
CMF C27 H38 N6 O6 S

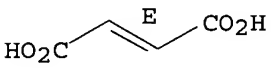
Double bond geometry as shown.



CM 2

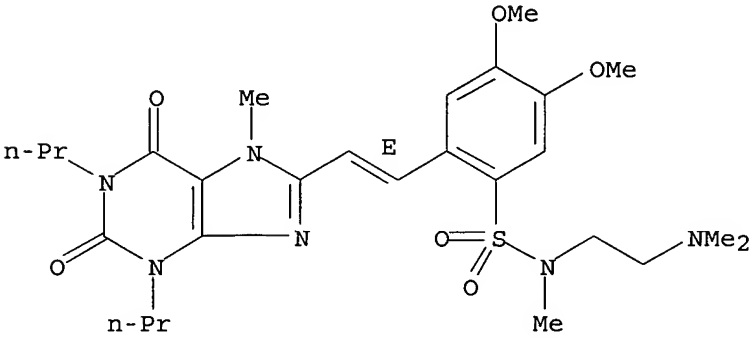
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 160434-15-1 HCAPLUS
CN Benzenesulfonamide, N-[2-(dimethylamino)ethyl]-4,5-dimethoxy-N-methyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

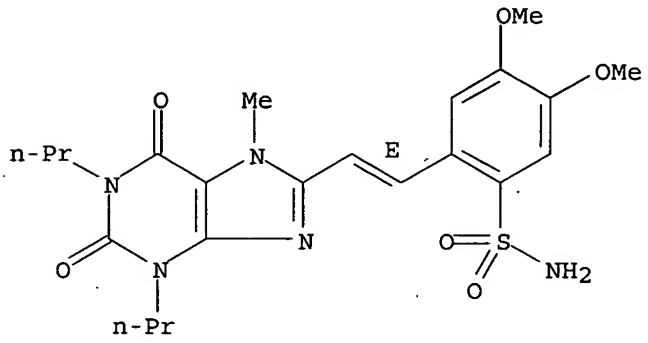
Double bond geometry as shown.



RN 160434-18-4 HCAPLUS

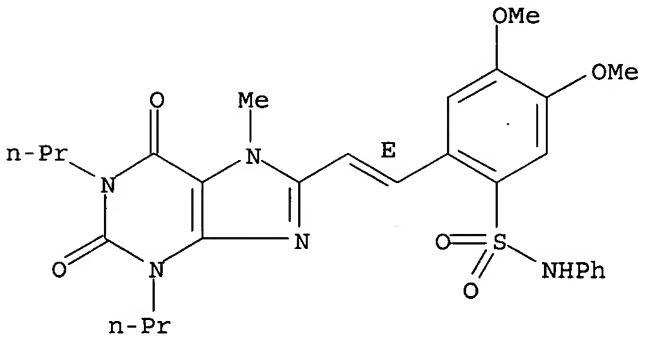
CN Benzenesulfonamide, 4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



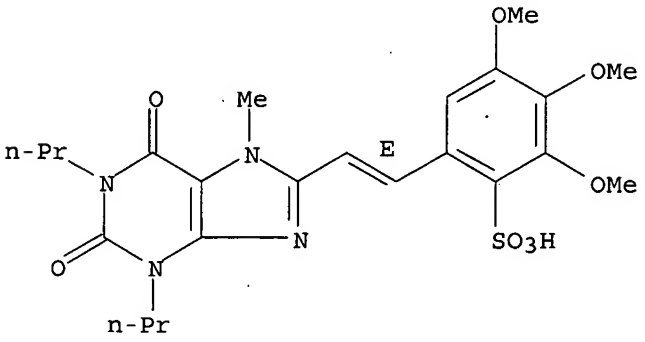
RN 160434-19-5 HCAPLUS
CN Benzenesulfonamide, 4,5-dimethoxy-N-phenyl-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



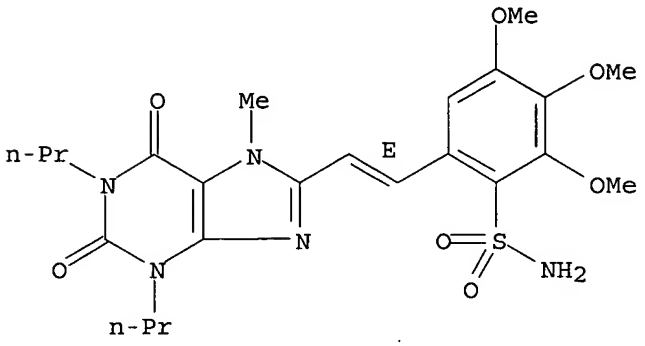
RN 160434-20-8 HCAPLUS
CN Benzenesulfonic acid, 2,3,4-trimethoxy-6-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 160434-21-9 HCAPLUS
CN Benzenesulfonamide, 2,3,4-trimethoxy-6-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

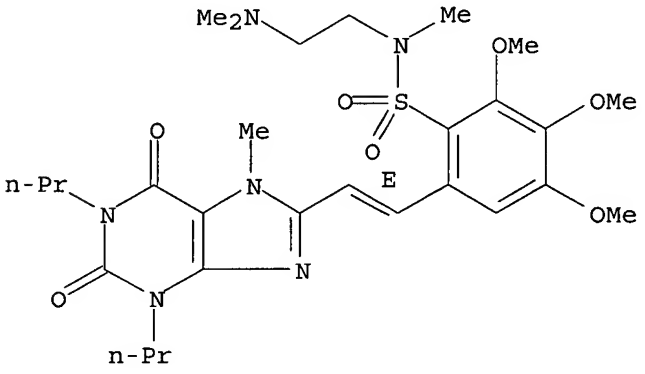


RN 160434-23-1 HCAPLUS
CN Benzenesulfonamide, N-[2-(dimethylamino)ethyl]-2,3,4-trimethoxy-N-methyl-6-[(1E)-2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 160434-22-0
CMF C28 H42 N6 O7 S

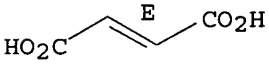
Double bond geometry as shown.



CM 2

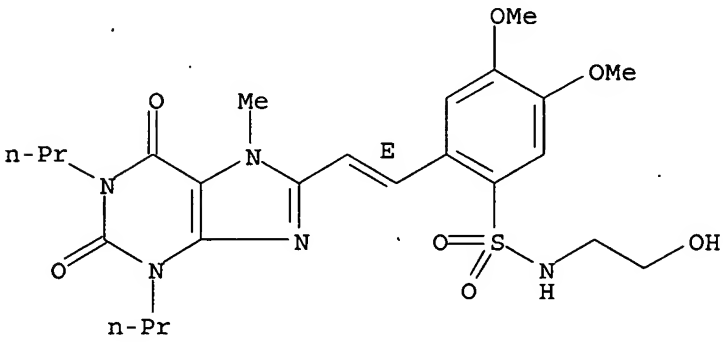
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 160434-24-2 HCAPLUS
CN Benzenesulfonamide, N-(2-hydroxyethyl)-4,5-dimethoxy-2-[2-(2,3,6,7-tetrahydro-7-methyl-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)ethenyl]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



L34 ANSWER 39 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:237592 HCAPLUS
DOCUMENT NUMBER: 122:23168
TITLE: Binding of [3H]KF17837S, a selective adenosine A2 receptor antagonist, to rat **brain** membranes
AUTHOR(S): Nonaka, Hiromi; Mori, Akihisa; Ichimura, Michio; Shindou, Tomomi; Yanagawa, Koji; Shimada, Junichi; Kase, Hiroshi
CORPORATE SOURCE: Pharmaceutical Res. Lab., Kyowa Hakko Kogyo Co., Ld., Shizuoka, 411, Japan
SOURCE: Molecular Pharmacology (1994), 46(5), 817-22
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential of 8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-[3H]methylxanthine ([3H]KF17837S) a a highly selective antagonist radioligand for the adenosine A2A receptor was examined and compared with the properties of the adenosine A2A receptor agonist radioligand 2-[p-(2-[3H]carboxyethyl)phenethylamino]-5'-N-ethylcarboxamidoadenosine ([3H]CGS21680). [3H]KF17837S specific binding to rat striatal membranes was saturable and reversible. Saturation studies showed that the binding of [3H]KF17837S occurred at a single site, with high affinity (Kd, 7.1 nM) and limited capacity (Bmax, 1.3 pmol/mg of protein). Adenosine receptor antagonist ligands competed with the binding of 1 nM [3H]KF17837S with the following order of activity: CGS15943 > KR17837S > N-[2-(dimethylamino)ethyl]-N-methyl-4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)benzenesulfonamide ≥ xanthine amine congener > 8-cyclopentyl-1,3-dipropylxanthine > 8-(noradamantan-3-yl)-1,3-dipropylxanthine > caffeine. Adenosine receptor agonists inhibited [3H] KF17837S binding in the following order: 5'-N-ethylcarboxamidoadenosine ≥ CGS21680 > 2-phenylaminoadenosine ≥ (R)-N6-phenylisopropyladenosine > N6-cyclopentyladenosine > (S)-N6-phenylisopropyladenosine. The Ki values of the antagonists for [3H]KF17837S binding and the rank order of potency were similar to those for [3H]CGS21680 binding. The affinities of the agonists were lower with [3H]KF17837S binding than with [3H] CGS21680 binding. However, a strong

pos. correlation (r = 0.98) was observed between the pharmacol. profiles for these two radioligand assays. The inhibition curve for CGS21680 was best fitted to a two-component binding model and addition of GTP shifted the inhibition curve to the right, suggesting that [3H]KF17837S labeled two agonist coupling states. Other pharmacol. agents had negligible affinities for the [3H]KF17837S binding site. Autoradiog. study of [3H]KF17837S binding using rat **brain** sections revealed that the binding site was highly enriched in the striatal region. The data indicate that [3H]KF 17837S labels the adenosine A2A receptor in rat **brain**.

CC 1-2 (Pharmacology)
Section cross-reference(s): 2, 8, 9

IT **Brain**
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

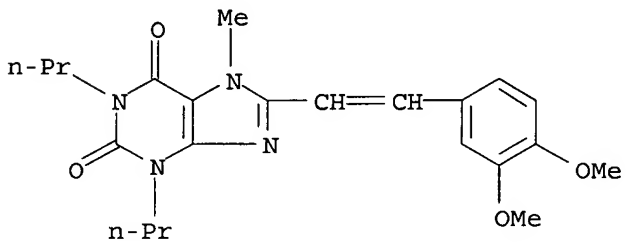
IT Neurotransmitter antagonists
(purinergic A2, characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

IT **149744-74-1**, KF 17837S
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

IT **149744-74-1**, KF 17837S
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of binding of selective adenosine A2 receptor antagonist [3H]KF17837S to rat **brain** membranes)

RN 149744-74-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)



L34 ANSWER 40 OF 40 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1994:571191 HCAPLUS
DOCUMENT NUMBER:	121:171191
TITLE:	Inhibition by KF17837 of adenosine A2A receptor-mediated modulation of striatal GABA and ACh release
AUTHOR(S):	Kurokawa, Masako; Kirk, Ian P.; Kirkpatrick, Karen A.; Kase, Hiroshi; Richardson, Peter J.
CORPORATE SOURCE:	Dept. of Pharmacology, Univ. of Cambridge, Cambridge, CB2 1QJ, UK
SOURCE:	British Journal of Pharmacology (1994), 113(1), 43-8 CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The effect of the A2A adenosine receptor agonist, 2-p-(2-carboxyethyl)phenethyl-amino-5'-N-ethylcarboxamidoadenosine (CGS 21680) on the potassium-evoked release of [3H]-GABA from nerve terminals derived from the caudate-putamen and the globus pallidus of the rat was compared. In both prepns. CGS 21680 (1 nM) inhibited the [3H]-GABA release evoked by 15 mM KCl but had no effect on that evoked by 30 mM KCl. The ability of CGS 21680 (1 nM) to inhibit the release of [3H]-GABA from striatal nerve terminals was unaffected by the presence of the GABA receptor antagonists, bicuculline (10 μM), phaclofen (100 μM) and 2-hydroxysaclofen (100 μM). Similarly the opioid receptor antagonist, naloxone (10 μM), the adenosine A1 receptor antagonist, 8-cyclopentyl-1,3-dipropylxanthine (DPCPX, 40 nM), and the cholinoceptor antagonists, mecamylamine (10 μm) and atropine (100 nM), had no effect on this inhibition. The ability of CGS 21680 (0.1 nM) to stimulate the release of [3H]-acetylcholine ([3H]-ACh) from striatal nerve terminals was unaffected by the presence of bicuculline (10 μM), 2-hydroxysaclofen (100 μM), phaclofen (100 μM), naloxone (10 μM) and DPCPX (4 nM). The novel A2A receptor antagonist, (E)-8-(3,4-dimethoxystyryl)-1,3-dipropyl-7-methylxanthine (KF 17837), blocked the CGS 21680 (1 nM)-induced inhibition of [3H]-GABA efflux with an EC50 of approx. 30 nM and also antagonized the CGS 21680 (0.1 nM)-induced stimulation of [3H]-ACh release with an EC50 of approx. 0.3 nM. It is concluded that the A2A adenosine receptor is present on both GABAergic and cholinergic nerve terminals of the rat striatum and that in both the caudate-putamen and the globus pallidus this receptor inhibits [3H]-GABA release. No evidence was seen for a difference in the ligand binding sites of this receptor in the 2 groups of nerve terminals.

CC 2-8 (Mammalian Hormones)

IT **Brain**
(globus pallidus, adenosine A2A receptor modulation of potassium-evoked GABA release from)

IT **Brain**
(neostriatum, adenosine A2A receptor modulation of potassium-evoked GABA release from)

IT **Brain**
(striatum, adenosine A2A receptor modulation of acetylcholine and GABA release from)

IT **141807-96-7**, KF 17837
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(adenosine A2A receptor-mediated modulation of acetylcholine and GABA release from striatum inhibition by)

IT **141807-96-7**, KF 17837
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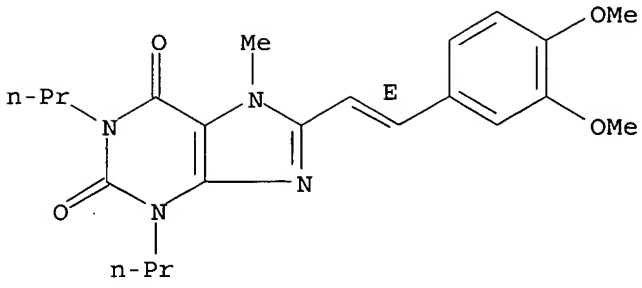
(adenosine A2A receptor-mediated modulation of acetylcholine and GABA release from striatum inhibition by)

RN 141807-96-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1E)-2-(3,4-dimethoxyphenyl)ethenyl]-3,7-dihydro-7-methyl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.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